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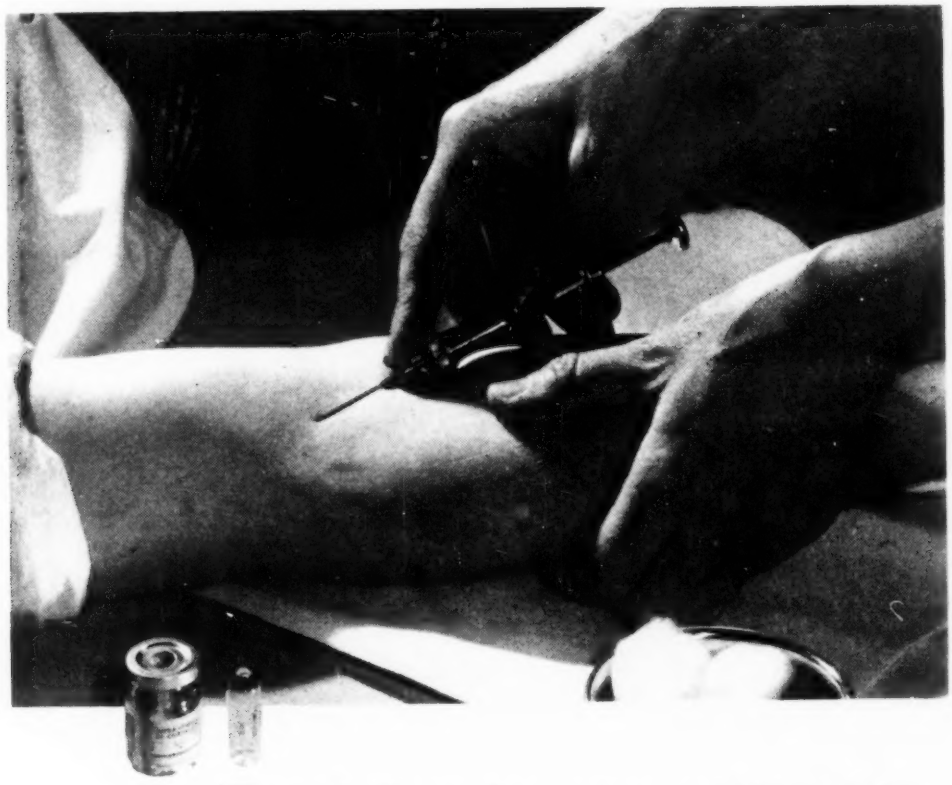

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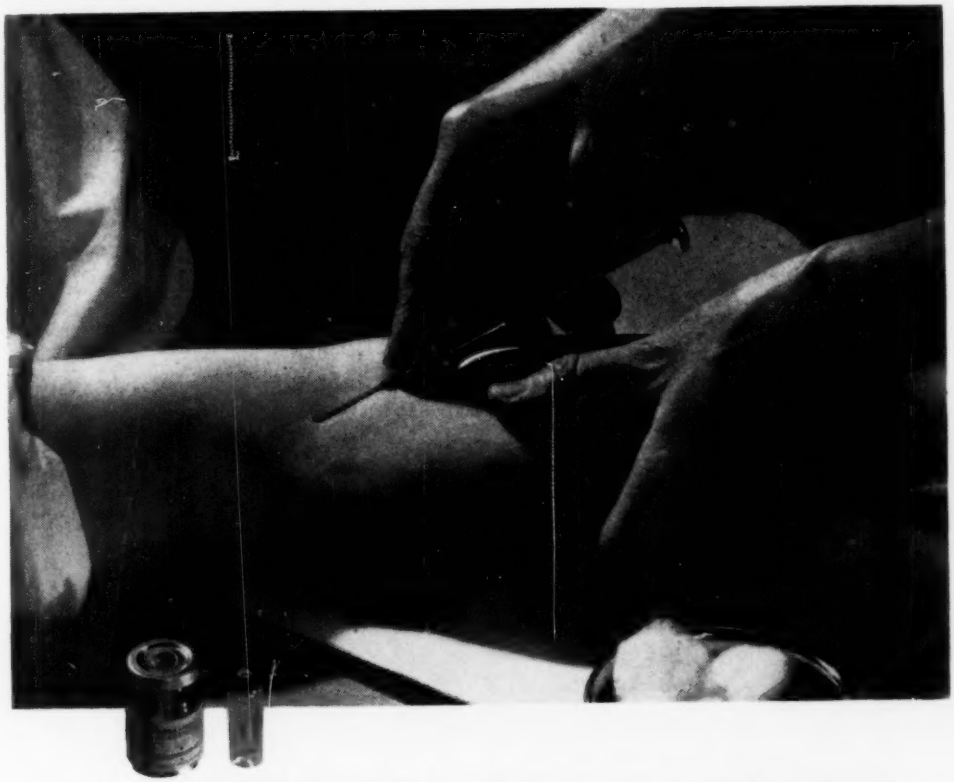

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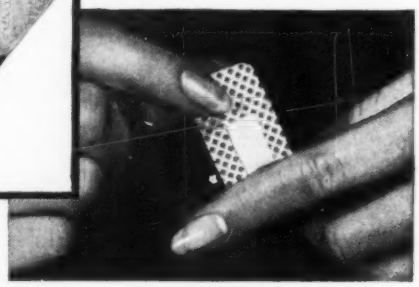

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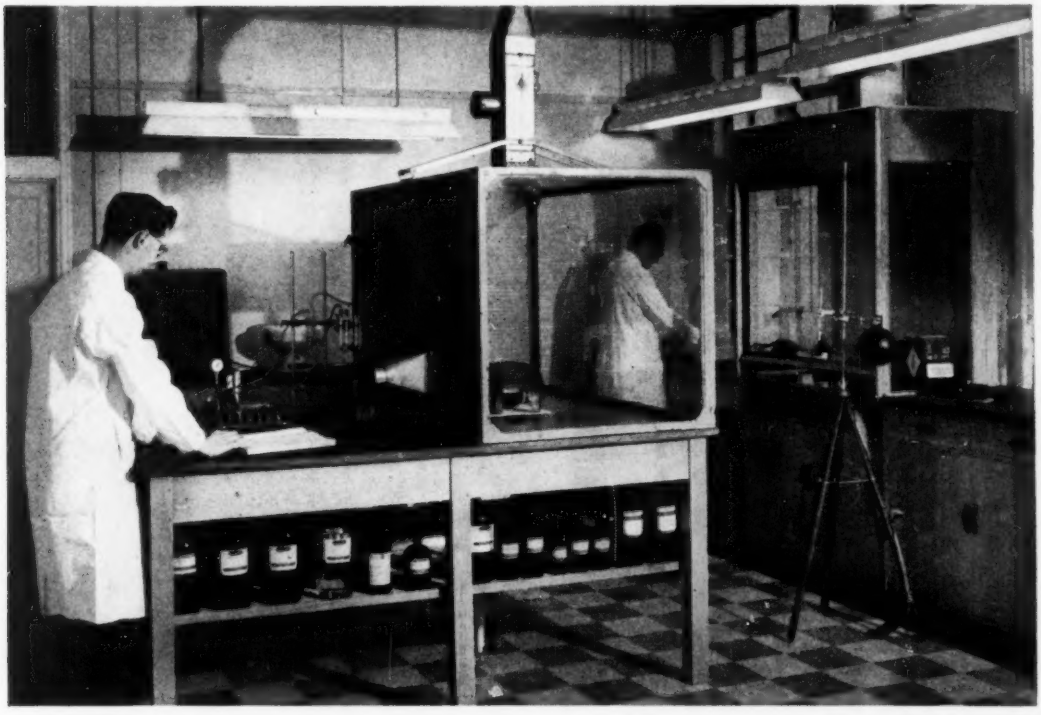

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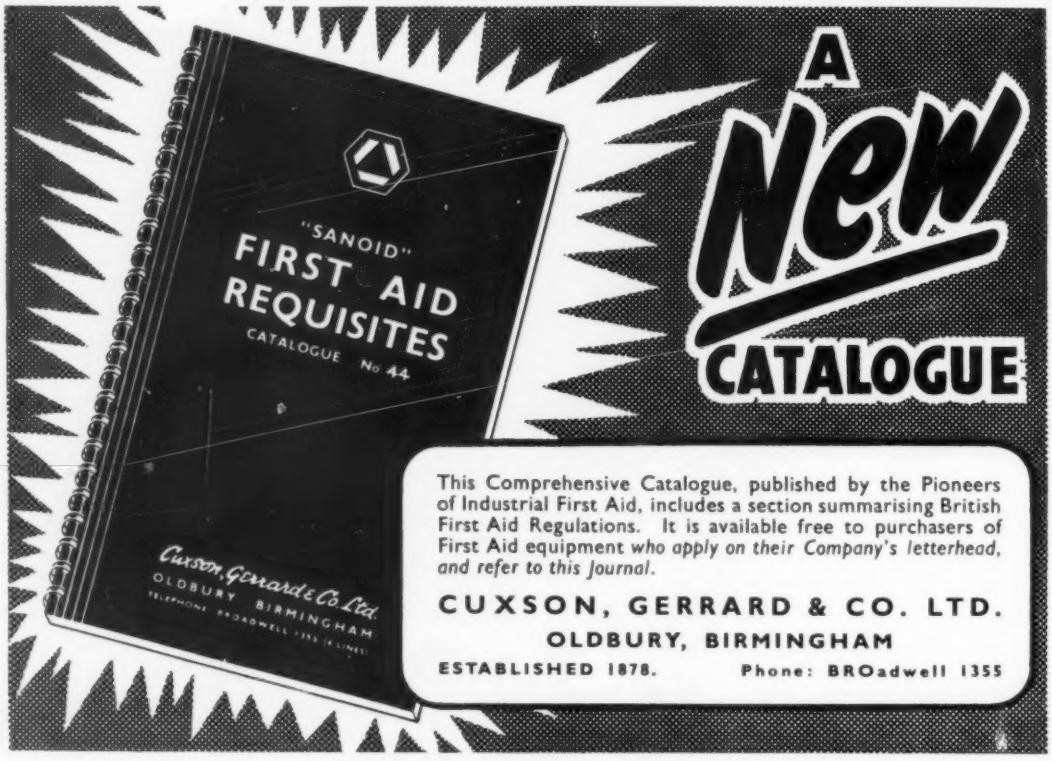
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INDUSTRIAL HEALTH—MEETING THE CHALLENGE*

BY

A. MEIKLEJOHN

From the Department of Industrial Health, University of Glasgow

(RECEIVED FOR PUBLICATION JULY 24, 1958)

The modern industrial system had its origin in England just over 200 years ago. This period historically is referred to as the Industrial Revolution. It was marked by mechanical inventions in textile machinery, by advances in the manufacture of iron, and by the introduction of steam power. These, in turn, were the foundations of the factory system.

In 1784 at a cotton mill at Radcliffe, near Manchester, an epidemic of malignant fever affected the operatives and spread to the surrounding population. The situation became serious and the local justices invited Dr. Thomas Percival, a leading local physician, to investigate the nature and circumstances of the outbreak. With his colleagues and leading citizens he formed the Manchester Board of Health. The Board, through authoritative reports, made recommendations for the control of such epidemics by the establishment of isolation hospitals. They also urged the need for the improvement of environmental conditions in mills and factories and for the diminution of working hours, especially for children and women. In pursuance of these objects the Government in 1802 passed the Health and Morals of Apprentices Act. This was the first Factory Act. Since then factory legislation has been greatly extended and is the basis of statutory supervision of factories and factory workers under the inspector of factories. The development of this supervision is traced with special reference to the work of the certifying surgeons, now the appointed factory doctors, and the medical inspectors. Concurrently, public health education and workmen's compensation were advanced through legislation. Since 1935 voluntary medical services have been developed in industry. These services have not been restricted to the observance of the minimum standards prescribed by statute and so have been able to pioneer advances directed to the promotion of safety, health, and welfare in factories and other places of employment.

Radcliffe, Percival, and steam power are recognized as the growing points of the challenge to health by the Industrial Revolution. The means whereby the challenge was met are discussed.

Towards the end of the nineteenth century scientists increasingly concentrated their studies on the elements. This culminated in the isolation of the atom. During the last 10 years atomic power has become a reality and the foundation of the second Industrial Revolution. While the potential hazards of ionizing radiations had long been known and proved at Hiroshima, the inherent dangers for the general population only became impressed on the public mind by a breakdown at the Windscale No. 1 plutonium pile on October 10, 1957. Radio-active iodine escaped, contaminating the atmosphere as far afield as western Europe. A committee under the chairmanship of Sir Alexander Fleck was appointed to investigate the cause of the accident and its consequences and to make recommendations. The report, which laid special emphasis on safety and health, was published early in 1958. So by analogy, Windscale, Fleck, and atomic power are identified as the growing points of the challenge of the Second Industrial Revolution. How this challenge is to be met by doctors is discussed. It is submitted that the urgent need is to formulate now a basic philosophy for future development of industrial medicine. Continuation of the old order will not suffice: ideas must again become revolutionary. The responsibility for leadership rests on the Industrial Health Advisory Committee established in 1955 under the chairmanship of the Minister of Labour and National Service.

*The Mackenzie Industrial Health Lecture of the British Medical Association delivered on July 15, 1958, at the University of Nottingham during the annual provincial meeting of the Association of Industrial Medical Officers.

PART I

The modern industrial system had its origin in England just over 200 years ago. This period is often indicted as among the darkest chapters in our social history, and in support of this charge contemporary records and documents provide ample evidence. But the suffering of young children and women induced by excessive labour, contagious and infectious diseases caused by unwholesome and insanitary conditions, and injury and deformity arising out of accidents due to unguarded machinery, did not pass unheeded. They presented an unremitting, inexorable challenge, a challenge which was met progressively by a system of inspection and supervision, under the force of law, directed towards the welfare, health, and safety of the factory worker. In this beneficent care of industrial communities we were pioneers. Since then we have remained in the forefront of thought and the advancement of knowledge in this field, though in practice we may have been surpassed by other countries. Nevertheless I am convinced that our present code of social legislation, which derived from these early tentative steps, represents the highest conception in the world to-day. Now on the threshold of the Second Industrial Revolution a new challenge, no less compelling than the first, confronts us, but:

> " Old England still throbs with the muffled fire
> Of a Past she can never forget:
> And again shall she banner the world up higher:
> For there's life in the Old Land yet."

The change from the domestic system to the factory system of manufacture and trade, which occurred in the eighteenth century, is generally referred to as the Industrial Revolution. That the change was violent is starkly expressed by Toynbee in his comment " the population were torn up by the roots ". The Revolution developed from a series of mechanical inventions commencing with Kay's fly shuttle in 1733 and culminating with Cartwright's power loom in 1785. While the new machines completely altered the traditional methods of cotton manufacture they did not of themselves constitute a revolution. This derived from two associated contemporaneous advances. The first was in 1760 when Dr. John Roebuck, a medical man, at Carron Ironworks near Falkirk in Scotland, succeeded in producing malleable iron by smelting with pit-coal. The second was nine years later in 1769 when James Watt, working as a mathematical instrument maker in the University of Glasgow, patented the condensing steam engine. A revolution in power resulted from the use of iron machines driven by steam. At first the power was applied as a pumping engine in the Cornish tin-mines but in 1785 Boulton and Watt, in partnership at Soho, Birmingham, made an engine for a cotton mill at Papplewick, near Nottingham. This was the critical advance, an engine which could drive machinery of all kinds. But steam could only be generated in a fixed spot and the power distributed over a small area. Consequently it was necessary to herd the workpeople close together in one building and those who, like the parish apprentices, had no homes, lived on the premises. As smallpox, typhus, typhoid, cholera, and other dysenteric diseases were endemic in England at this period, it was no accident that these factory communities were ravaged by disease. Epidemics were common and it was inevitable that sooner or later one of these would break the factory bounds and involve the whole surrounding population. So it happened in 1784 at a mill owned by Sir Robert Peel (the elder) at Radcliffe near Manchester.* In a Short Essay written for the Service of the Proprietors of Cotton-Mills and the Persons employed in Them (anonymous: Manchester, 1784) it is recorded that:

> " It is a well-known fact that there has been a contagious disorder in a cotton mill in the neighbourhood of Manchester, which has destroyed many persons, and endangered the lives of more."
>
> " With respect to the nature of the disease, it was a malignant fever . . . it generally ran through whole families, equally affecting people of all ages, but most fatal to the men . . . and it was similar to the fevers that frequently rage in jails, ships and hospitals."

The outbreak of fever involved the whole locality and from contemporary reports it was particularly widespread and virulent in Salford. The local justices, compelled to face the challenge, invited Dr. Thomas Percival, a Manchester physician, to investigate the nature and the circumstances of the outbreak. He reported that the epidemic was due to overwork for inordinately long hours, poor food, wretched clothing, bad ventilation, and overcrowding in insanitary houses and factories. especially by children. Percival continued his enquiries, enlisting the help of a very able young colleague, Dr. John Ferriar (Greenwood, 1948). With leading local citizens and physicians they formed the Manchester Board of Health (1805). At the first meeting held at the Bridgewater Arms Inn, Manchester, under the chairmanship of T. B. Bayley, Esq., on January 7, 1796, Percival defined the objects of the Board as threefold:

(1) To obviate the generation of diseases.
(2) To prevent the spreading of contagion.
(3) To shorten the duration of existing diseases, and to mitigate their evils, by affording the necessary aids and comforts to those who labour under them.

*A reprint of the original report by Dr. Thomas Percival and colleagues 1784, is published on page 68 of this issue.

Ferriar in turn enunciated a fundamental proposition:

> " The safety of the rich is intimately connected with the welfare of the poor, and a minute and constant attention to their want is not less an act of self-preservation than of virtue."

Percival submitted five resolutions for deliberation by the members of the Board of Health in formulating preventive measures. The first four embrace the purposes defined in the objects of the Board. This is the final item:

> " From the excellent regulations which subsist in several cotton factories, it appears that many of these evils may, in a considerable degree, be obviated; we are therefore warranted by experience and are assured we shall have the support of the liberal proprietors of these factories, in proposing an application for Parliamentary aid (if other methods appear not likely to effect the purpose), to establish a general system of laws for the wise, humane, and equal government of all such works."

This was the first proposal for an organized attack on vicious conditions in mills and factories and against bad employers. Percival, however, it will be noted, mentions good employers, who maintained satisfactory conditions of labour and so provided a model. The magistrates at Manchester immediately took action and were supported by their colleagues in other large factory areas. In 1802 the Government, faced by this situation, passed an Act for the Preservation of the Health and Morals of Apprentices and Others employed in Cotton and Other Mills and Cotton and Other Factories.

In practice the Act proved quite ineffective but it represented an important advance, namely, the right of the Legislature to interfere in the regulation of the conditions of industrial employment. During the ensuing 30 years practically no progress was made, but meanwhile the damning evidence against factory conditions was relentlessly accumulating.

Ultimately, a Select Committee under the chairmanship of Michael Sadler, a flax mill owner and Member of Parliament for Leeds, was set up in 1831 to enquire into the conditions of children in factories. The Report (1831), one of the most human documents of all time, was rejected by Parliament as a basis for new legislation. Two years later, however, a Royal Commission on the Employment of Children in Factories was appointed. The Commissioners, who included leading physicians, visited all factory areas to obtain evidence at first-hand. Dr. Charles Loudon, medical commissioner for the North Eastern District, concluded his Report thus:

> " I would compel the occupier of every mill to appoint a medical officer to his or her factory, who would examine every child before admission, to see whether its constitution was such as to bear the work; and this medical practitioner should visit the mill at least once a week, or oftener, to ascertain the health of the operatives generally; to this person I would consign the hygienic as well as the medical care of the factory. Besides attending to the sick of all classes in and out of the mill, it would be his business to see that the building was thoroughly washed with quicklime and water at certain periods of the year; that the windows were properly constructed to admit fresh air; the drains and water closets in proper order; the floors kept properly clean, and the machinery carefully boxed off."

Dr. Williamson of Leeds advised that " if possible every mill should be provided with baths for both sexes ".

Following a Bill introduced by Lord Althorp, Parliament, on August 29, 1833, passed an Act to Regulate the Labour of Children and Young Persons in the Mills and Factories of the United Kingdom (Factory Inquiry Commission, 1833). The employment of children under the age of 9 years was prohibited and persons under 18 were not to be allowed to work at night or for more than 12 hours a day, excluding meal-times, in mills or factories. Furthermore children were not to be employed without the certificate of a surgeon as to " strength and appearance ".

As proved by subsequent events section 17 was the keystone, namely, " Four persons to be appointed to be Inspectors of Factories and Places where the labour of Children and Young Persons under Eighteen years of Age is employed ".

Section 20 which required children in factories to attend school was no less important.

Robert Saunders, Robert Rickards, Thomas Howell, and Leonard Horner were appointed to be the first four district inspectors and later they were assisted by superintendent inspectors. All four immediately entered on their onerous and difficult duties with great zeal, indeed with a missionary spirit. To ensure uniformity of practice and administration they met, as prescribed, in conference every six months and each prepared a quarterly report on his work. These reports are very full and informative and remarkable for their critical outlook and constructive practical recommendations for improvement. The inspectors emerge as men of integrity and great moral courage.

Rickards, whose district comprised Lancashire and Yorkshire, resigned on account of illness in 1836. Horner, who had been in charge of Scotland and Ireland, was transferred to succeed him. It is of interest to note that in his quarterly report dated September 20, 1836, he refers to " Mr. Baker, surgeon of Leeds, the factory superintendent in that division of my district ". Before his appointment as a superintendent inspector, Robert Baker started

to practise as a doctor and Poor Law medical officer in Leeds in 1825, and so was a contemporary and neighbour of Charles Turner Thackrah.

The inspectors unanimously urged the extension of the Act to silk and other mills and factories. Leonard Horner was not only a distinguished scientist, a Fellow of the Royal Society, and of the Geological Society, of which he became president, but he was also a leading educationist. He regarded individual factory schools as inadequate and advocated that employers should combine to establish central or joint schools. In this advancement of child education he was strongly supported by Howell, who recorded that " in some small mills the master himself is frequently unable to read or write (in Wales he very often cannot even speak English)".

Saunders concentrated his attention on the surgeons' certificates of age. He was concerned to ensure their validity and prevent fraudulent use by employers and parents. To define criteria of the ordinary strength and appearance related to age he instituted an enquiry into physical measurements of children in various districts. When he sought to establish the development of teeth as a test of age for persons between 7 and 14 years of age he was opposed by many surgeons. He also foresaw the need to restrict the issue of certificates to specially appointed surgeons. This was his conclusion (Saunders, 1838):

> " When medical gentlemen will faithfully and conscientiously perform their duty, I am convinced it would be impossible by any other means yet suggested to secure to the younger classes as effectually the protection extended by the Legislature."

Saunders' aim was achieved in 1844 by the passing of an Act to amend the laws relating to labour in factories. This Act empowered the inspectors to appoint in each district a sufficient number of persons practising surgery or medicine to be certifying surgeons to give surgical certificates of age. The examinations were restricted to them and were to be made at the factory. An added duty was to examine the causes and extent of accidents and to report thereon to the district inspector. These provisions marked the beginning of statutory medical services in factories. So after 60 years the challenge of Radcliffe was slowly but progressively being met in the cotton mills and factories. Meanwhile sanitary science under the leadership of Edwin Chadwick had proved a powerful ally, and through the care of water supplies, disposal of sewage, and the provision of isolation hospitals had begun to advance the public health. Concurrently, the education of children was extending in factory and national schools. In short, the foundations had been laid of statutory medical supervision in factories, of public health, and of popular education.

The next phase, extending over nearly 50 years, was marked by see-saw amendment and consolidation of the system and its administration, including extension to all varieties of textile mills and factories and non-textile factories and workshops. The payment of compensation for accidents at work not only gave some financial relief to workmen and their dependants but assisted indirectly towards the prevention of mishaps. Parallel legislation, though delayed, developed for control of work in coal-mines. So far the challenge comprised adverse social conditions, community diseases and accidents. Finally a new problem, which had been increasingly recognized, thrust itself to the forefront: this was industrial or trade diseases.

Trade Diseases

From their intimate experience of workmen and workplaces the certifying surgeons made notable contributions in this field. Moreover, as the majority of the surgeons were local general practitioners they knew the suffering and tragic hardships which accompany chronic disease, disablement, and premature death. I can only cite briefly a few outstanding examples of these contributions.

Charles Purdon (1819-1882), certifying surgeon for the Belfast district, recorded the various affections of operatives in flax mills and linen factories. Mill fever he attributed to " the smell of oil along with vapour and heat of the room ". His description of the clinical picture and course of asthma due to the inhalation of pouce, fine flax dust, is still unsurpassed. The condition, byssinosis, is nowadays more generally associated with work in cotton mills. Among other conditions which he noted in these workers was a peculiar eruption which attacked uncovered parts of the body. To this he gave the name lichen and remarked that he had never seen a case in an adult. He attributed this form of occupational dermatitis to the effect of flax water, which also caused onychia of the toes, a common complaint due to the custom of working barefoot.

William Francis Dearden (1863-1931), of whom it was said that he was " first of all a Lancashire man and then a doctor ", devoted his life to the study of occupational hazards in the cotton industry. His observations were embodied in the Milroy Lectures delivered before the Royal College of Physicians of London in 1927, entitled " Health Hazards in the Cotton Industry ". In turn he served as secretary and president of the Association of Certifying Factory Surgeons and he wrote several excellent

brochures on the functions of a factory medical service.

In the course of his practice as a certifying surgeon and consulting physician to the North Staffordshire Infirmary John Thomas Arlidge (1822-1899) devoted his life to the study of diseases, particularly chest diseases, of potters and colliers. His observations were embraced in the Milroy Lectures of 1889. These lectures were the foundation of his book on the "Hygiene, Diseases, and Mortality of Occupations", a work which will stand comparison with all similar works, past and present. Incidentally, it is of interest to note in passing the admirable contributions to industrial diseases made by a long succession of distinguished Milroy lecturers. I shall recall only two others, R. Prosser White (1915), of Wigan, the author of "Occupational Affections of the Skin", and Alexander Scott (1922), of Broxburn, another pioneer in the field of the dermatoses and skin cancers, particularly those associated with exposure to paraffin in the Scottish shale oil industry.

In 1898 Dr. Legge (later Sir Thomas Legge) was appointed to be the first medical inspector of factories. In conjunction with Dr. Oliver (later Sir Thomas Oliver) of Newcastle-upon-Tyne and Dr. Goadby (later Sir Kenneth Goadby) he laid the foundation of the systematic study and prevention of occupational diseases as described in his book "Industrial Maladies" (1934). His name will always be linked with the control of anthrax and lead poisoning. The branch of the factory inspectorate which he initiated has added greatly to our knowledge of industrial diseases: Collis, Middleton, and Merewether in the field of dust diseases of the lungs, Henry on occupational skin cancer, and Ethel Browning on chemical intoxications. The present members of the staff have also made notable contributions and with their colleagues are worthily maintaining a great tradition.

Dr. John C. Bridge (1945), who succeeded Sir Thomas Legge on his resignation in 1926, initiated a new application of medicine to industry, namely, the modern system of medical supervision. The development of this owes much to the pioneer work of Dr. A. J. Amor and his colleagues at the Ministry of Supply during the Second World War and to such outstanding medical officers in private industry as Dr. Leonard Lockhart, Professor R. E. Lane, Dr. Donald Stewart, and Dr. Austin Eagger. The impact of all these contributions is variously reflected in the Tomlinson (Cmd. 6415, 1943), Gowers (Cmd. 7664, 1949), and Dale reports (Cmd. 8160, 1951).

Throughout this period of 60 years industrial diseases have been increasingly linked to problems of workmen's compensation. Pneumoconiosis has dominated this aspect and none has served better in the study of the hazard in specific occupations, in the development of legislation and its administration than Dr. Charles L. Sutherland.

In this review I have concentrated on doctors and factories, but this does not signify that I underrate the great, in some respects greater, contributions of the social reformers, statesmen, administrators, far-sighted employers, workers' leaders, and research workers. Nor am I unmindful of those who have concurrently so successfully promoted public health and the safety, health, and welfare of coal-miners. The story of the answer to the challenge of the Industrial Revolution is seen as one of halting progress, of practice trailing behind knowledge, of the inspectorate enforcing observance of minimum standards prescribed by law, while the voluntary system of medical supervision in private industry has experimented with new techniques and so paved the way to fresh advances. But not all private industry has participated nor is there any real evidence that all employers will do so either by invitation or recommendation. This leads me to the second part of my theme.

PART II

While social reformers, legislators, and administrators, lay and medical, were striving to advance the safety, health, and welfare of workers in factories and mines, almost unperceived by them chemists and physicists were more and more speculating on the genesis of the elements. In 1888 Sir William Crookes spoke of "an infinite number of immeasurably small, ultimate, or rather ultimatissimate particles gradually accreting out of the formless mist, and moving with inconceivable velocity in all directions". In the light of current knowledge we may aptly quote:

> "Often do the spirits
> Of great events stride on before the events.
> And in to-day already walks to-morrow."

I am not competent to describe the work of such notable scientists as Planck, Einstein, the Curies, Rutherford, and Bohr, which led to the discovery of atomic power and its application to peaceful industrial processes. Over many years electricity generated by coal and water power had steadily increased mechanization in industries but the advent of atomic power signifies sudden and violent changes in methods of work and production. Indeed so great, in fact and in potential, is this change that it represents a second Industrial Revolution.

The dangers of ionizing radiations, well known to medical men often from bitter personal experience, became generally known after Hiroshima. Not

unnaturally, increased industrial use caused widespread apprehension. Meticulous precautions were taken to safeguard the workers employed in atomic plants. The cost of absolute protection, if possible, was prohibitive and an international conference of experts recorded the need to accept a calculated risk. Public anxiety was largely latent until the radiation hazard broke bounds. On October 10, 1957, due to a breakdown at the Windscale No. 1 plutonium pile, radio-active iodine escaped through the filters of the two 400-feet-high chimneys, contaminating the atmosphere and pastures over an area of nearly 200 square miles. Possible adverse effects on the local inhabitants were almost immediately suggested by the detection of a rising concentration of radio-active iodine in cow's milk.

The United Kingdom Atomic Energy Authority acted promptly by setting up an expert committee under the chairmanship of Sir Alexander Fleck to investigate the cause of the accident and its consequences. The Committee was also charged: " To review the organization within the Authority as a whole for control of health and safety and to make recommendations ". History was repeating itself. In 1784 the growing points of the challenge were represented by steam, Radcliffe, and Percival; in 1957 by the atom, Windscale, and Fleck. On this occasion, however, circumstances are vastly different. In 1784 the challenge comprised the excessive labour of children and young persons for 60 hours a week or more ; undernutrition and malnutrition ; grossly insanitary conditions; acute infectious diseases and physical strain; and illiteracy. The workers had not combined in trade unions. By 1957 all these matters had been substantially remedied or at least ameliorated. By contrast the new challenge includes the ageing population and the elderly workman; the use of leisure associated with the 48-hour week diminishing to 40 hours; mental stress; maintenance and promotion of health; rehabilitation and resettlement of persons handicapped from any cause; and technical education. Trade unions are now among the most powerful organizations in the country. On the previous occasion there was no experience to guide the reformers. This time we cannot plead such handicap. How then do we view the new challenge and by what means shall we meet it ?

The historical development of factory legislation proves that the foundations of the statutory system of inspection and supervision were substantially laid in the 10 years immediately following the first appointment of factory inspectors in 1833. The succeeding 100 years were marked by a tentative, halting extension of the system assisted by concurrent advances in public health. This signifies that over the next few years we must endeavour to envisage the whole challenge which confronts us, so that we may establish a basic philosophy to meet it. The responsibility for leadership devolves on the Industrial Health Advisory Committee set up by the Minister of Labour and National Service in 1955. It is important that the Committee should recognize and accept this responsibility and that we should constantly press for practical results. A start has been made; the Halifax Report published in March, 1958, is the first fruit of their work.

I have already suggested that we are at the beginning of a second Industrial Revolution, which, like its predecessor, presents a challenge in the field of industrial health. Straightway I would underline that a gradual linear extension of the previous system will not suffice; we must again become revolutionary in our ideas.

Factory Inspectorate

The Factory Inspectorate has proved its worth and provides a sound foundation for future developments. Right from its inception it has constantly been argued that relative to the size and composition of industry the number of inspectors is inadequate. Recently there has been an increase but it is clear that the establishment, even if multiplied several times, would still not assure constant effective supervision of all places of employment. Perhaps the solution is a new strategy of inspection, whereby the available staff is deployed to greater advantage. One need is urgent and paramount, namely, laboratory facilities. The establishment of regional occupational hygiene units for the use of the inspectors and to provide a consultant service for private industry is long overdue. Moreover, the basis of such a development already exists in the Public Health Laboratory Service, which to a large extent has become redundant since the introduction of the National Health Service. This is an aspect of industrial health in which the local authority health services could contribute with advantage. Similar opportunity for cooperation exists in the provision of radiological facilities for the work of the medical inspectors.

The Appointed Factory Doctor

The appointment of the certifying surgeons in 1844 was the beginning of statutory medical services in industry. By reference to the work of a few I have sought to indicate the excellent contributions which they made to safety, health, and welfare in factories. However, as appears from reports of parliamentary proceedings, from evidence to committees and commissions and from comments in medical journals their work was frequently condemned as negative, narrow, and cursory. As an example the Editor of

the *Glasgow Medical Examiner* in June, 1869, described their work as " services wholly unworthy of being called professional ". At this time an extension of the Factory Act was under consideration and the senior inspectors were Mr. Arthur Redgrave and Mr. Robert Baker. Redgrave was critical of the certifying surgeons and sought to abolish them but was opposed by Baker who, it will be recalled, had formerly practised as a doctor in Leeds. The *British Medical Journal* supported the surgeons; the *Lancet* was against them. Much of the criticism was justified and in a measure is still applicable. But the important point is that basically the fault did or does not lie in the surgeons but in the system which prescribes their duties. The doctors have always regarded the official scale of fees as inadequate and appropriate only to rapid cursory fulfilment of the prescribed duties.

Consideration of the work of the certifying surgeon, now appointed factory doctor, must include reference to the School Health and Youth Employment Services. The whole subject was carefully examined by a Departmental Committee, whose Report on Medical Examination of Young Persons for Factory Employment was published in 1924 (Cmd. 2135). The Committee made many recommendations, several of which have since been implemented. This was the principal recommendation which was printed in bold, heavy type:

> " Local Authorities should at once be invited to submit schemes for taking over such examination and certification of young persons, and that the aim in view should be that if the voluntary trial made by Local Authorities proves successful, the transfer of the whole of this work should be ultimately effected by Order of the Departments concerned."

Now more than 30 years later this change has not been effected. I do not mean to signify that I agree with the recommendation but my purpose is to emphasize that this is an aspect of the system which demands urgent re-examination with a view to improvement and simplification of the medical supervision of young persons.

The Committee also recommended that the age for examination should be raised from 16 to 18 years. This has now been done, but the then Chief Inspector of Factories, Mr. Gerald (later Sir Gerald) Bellhouse, stated in a personal memorandum that he " was exceedingly doubtful as to the necessity for raising the age for examination ".

Careful study of the Report makes if difficult to avoid the conclusion that a necessary advance was hindered by the rivalries and power complex which seem to afflict departments of state. However, the medical examination of young persons, whatever their occupation or place of employment, is a fundamental element of the present challenge. It must be met effectively. Professor Lloyd Davies, while engaged as an industrial medical officer here in Nottingham, proved by his outstanding work what can be achieved in this vital area between school and early years of employment. Dr. Martin Herford (1957), an appointed factory doctor, by his own work, forthright criticisms and recommendations for improvement has tried to focus attention on the subject. More recently Lee (1958) has cast grave doubts on the effectiveness of routine examination of school children by the school health service. The fact which emerges is that the school medical officer and the appointed factory doctor are each shackled to a system in which there is not sufficient time for effective or satisfying work. It is little wonder that defects, often remediable, are overlooked. The truth is that the whole medical body is suffering from a creeping paralysis of good clinical work due to a progressive, often purposeless proliferation of routine examinations.

This is not the place to discuss new arrangements for the examination of school leavers and new entrants to employment. However, I have already indicated that the scheme should embrace all young persons and I would suggest that the appropriate place and time would seem to be at school, as close to the age of 15 as possible, that is while pupils are easily accessible to facilities for complete examination. This might be the critical step towards integrating the work of the appointed factory doctor and the school medical officer. It might also be the means of utilizing the services of a much larger number of general practitioners and establishing through these three groups under the direction of the medical inspectors a service for small factories, shops, offices, and other places of employment.

Medical Inspectorate

The scope, functions, and duties of the medical inspectors seem soundly based and Legge and his successors have, as I have mentioned, made notable contributions to industrial health, particularly in the field of occupational diseases. And this has been achieved in spite of the handicap of inadequate laboratory facilities for clinical and environmental investigations. There are two further matters which I wish to stress here. The first concerns nurses in industry, the backbone of most medical departments. In 1951 I ventured to advocate the appointment of nursing inspectors. At the I.L.O./W.H.O. seminar on the " Nurse in Industry " held last year in London this idea was discussed and supported. I hope that the Industrial Health Advisory Committee will give this matter careful consideration. Secondly,

the medical inspectors should conduct regular courses and conferences to advance and coordinate the work of the appointed factory doctors.

Voluntary Medical Services

In the future development of medical services in industry the Report of the Fleck Committee (Cmd. 342, 1958) is, I believe, the most significant document of our times. Admittedly, it was directed to the control of health and safety from the hazards of atomic energy but if we insist on construing it thus narrowly and fail to realize its wider connotation then we shall stand condemned by future generations. We shall have failed to meet the challenge of occupational health and safety and not only in our own country but throughout the world. We are our brothers' keepers.

The Fleck Committee in propounding their basic philosophy underlined that the special problems of atomic energy require that the preparation of codes of practice for design and operation should be the responsibility of specialized health and safety staff, and that attention should be given to standards of occupational and non-occupational exposure to radiation and to toxic materials associated with nuclear reactors, process plants, and laboratories. Among the important recommendations which they made are the building up of a supply of specialist medical staff for the control of health and safety and that a national training centre for health physics and nuclear safety should be established. The United Kingdom Atomic Energy Authority have already started to implement these recommendations. This scheme, suitably adapted, can be the prototype for all industries.

The difficulty of applying any scheme to the whole of the employed population is, as has so frequently been emphasized since the Dale Report, that industry is largely made up of small occupational groups. In the Halifax Report the Industrial Health Advisory Committee made this significant comment:

> "The right plan would seem to be to proceed by stages. The first stage should be to approach the occupiers of those factories in Halifax where 250 or more workers are employed with a view to interesting them in the advantages of the provision or extension of medical and nursing services."

The Committee listed the main elements in such a service. This recommendation is a vital response to the present challenge. But recommendation is not enough; the legislature should forthwith announce their intention to require all units of this size to provide such a medical service. In Norway it has already been proved that this can be achieved on the basis of the attendance of a doctor for a minimum of one hour per week per 100 workers. The doctor, I believe, should be appointed and paid by the employers for, as so admirably expressed by Duncan (1958), only thus shall we attain a "personally aimed service, flexible and not strangled by mere observance of minimum standards" and restricted to routine examinations. As in the past this free service will experiment and provide a pattern leading to progressive advance. And in such appointments the doctor need not fear insecurity; a nation-wide industrial medical service will give security and opportunities for promotion through freedom of choice of job. For many reasons it is clear that such extension cannot be imposed and enforced immediately. This is an advantage; indeed it is desirable that the effective date should be post-dated by at least one year.

Education and Training

The fixing of the appointed day well in advance is fundamental to enable doctors, who intend to seek appointments, to attend short courses of instruction in the principles and practice of industrial health. Indeed, it would be invaluable if it were made a condition that no doctor will be eligible for appointment, including that of appointed factory doctor, until he can produce evidence that he has attended such a course. The omission of such a recommendation was, in my opinion, a defect of the Halifax Report. Moreover, failure to realize this very need in the appointment of disablement resettlement officers has hindered the efficient operation of the Disabled Persons (Employment) Act since its enactment in 1944.

In March, 1957, the Joint I.L.O./W.H.O. Committee on Occupational Health published a report (Tech. Rep. Series No. 135, Geneva) on the training of doctors in occupational health and on the scope and organization of occupational health institutes. Despite the experiments of the Nuffield Foundation in this field over a period of 10 years, the faculties of medicine have so far failed to pronounce as a result of this experience on the place (if any) of departments of industrial health in the universities and associated medical schools. This situation, however, would not be a matter of serious concern if there was any real evidence that a patient's employment in relation to his physical and mental condition was being adequately dealt with in clinical teaching. Examiners for higher qualifications could make an immediate contribution through written, clinical, and oral questions.

The Medical Department in Industry

I do not propose to review the working of the medical department but there are a few matters to

which I should like to allude briefly. The department must recognize health education of both management and workers as a primary function. Management has a duty to understand the purpose of the department and to ensure that it is efficient. Shop stewards must assist more actively in enforcing on their members full compliance with all measures for safety, health, and welfare. Sir Thomas Legge may have been right in his assertion that the workman is naturally enough willing to do his share to protect himself; in the future he must do a great deal more than what he interprets as his share at present.

It is often argued that a firm has not sufficient work to employ a doctor fully or substantially part time. This attitude derives from a focus on accidents and sickness and without regard to prevention. I venture to submit that the most important item is to assure that the doctor has free time—time to think, study, review, and apply his experience gained in the surgery and on the plant. Only thus can he hope to diminish the number of patients and so have adequate time for proper investigation of each case, the basis of which is time to listen attentively and observe carefully. And let us recognize that the emergency treatment of casualties and occupational diseases is relatively unimportant, compared with the detection of minor deviations from health of body and the mental effects of stress not only in individuals but in the group, in which no demarcation can be made between the influence of work and other activities.

Cost of Industrial Health Service

Eight years have now elapsed (and the choice of " elapsed " is intentional) since the Dale Committee (Cmd. 8170, 1951) reported that:

> " In our view it is desirable that there should eventually be some comprehensive provision for occupational health, covering not only industrial establishments of all kinds, both large and small, but also the non-industrial occupations . . . This, however, is a long-term view which cannot be made effective without much more experience to be gathered from future surveys and experiments."

This proviso about surveys and experiments was reasonable but there is a danger that it may become an alibi in defence of indecision and procrastination.

Even if this comprehensive provision for occupational health, complementary to the National Health Service, is desirable, it will be argued that at this period of financial stringency industry cannot afford it. Many more skilled than I have discussed the price of health and the cost of sickness. Still I would direct attention to current experience of the National Insurance and Industrial Injuries Funds as presented in the Annual Reports of the Ministry of Pensions and National Insurance (H.M.S.O., London). In the years 1951-1952 contributions from employers and insured persons to these funds amounted to £447,506,000 and increased to £610,079,000 in 1955-1956. During these years the corresponding figures for sickness benefits were £63,301,000 and £99,642,000 and for industrial injuries £16,325,000 and £32,063,000. Even allowing for increased rates of benefits these figures represent substantially rising costs. Furthermore, the trend of claims, particularly for minor sickness and injuries, is progressively upwards. So far rising costs have been met by the simple device of increasing contributions but these are now at a level which hurts. It must also be remembered that the funds are supplemented by annual contributions from the Exchequer. In respect of the Industrial Injuries Fund this supplement rose from £6,039,000 in 1951-1952 to £8,100,000 in 1955-1956. These costs, reflected in increased contributions, will go on rising and steeply if, as experience proves, there is unemployment and industrial unrest. I believe medical supervision in industry to be a major constructive approach to health and consequent saving on sickness and injury benefits. But this is not the real issue, for as so cogently expressed by Herbert Spencer:

> " The preservation of health is a duty. Few seem conscious that there is such a thing as physical morality."

Preservation is not enough, we have a duty to promote health. This has been named " positive health ", a term which has been criticized because of lack of precise definition. I know of none better than the words of our Lord:

> " I am come that they might have life and that they might have it more abundantly."

CONCLUSIONS

In the course of this lecture I have said many things which are heterodox; indeed to some of you rank heresy. If this is so then I may have excited you to thought and argument and that is the real purpose of education, the purpose to which James Mackenzie dedicated his life. From thought, progression is to study and so to knowledge and finally to action. Never before in history has the science of medicine given us so many tools with which to bring to all men new vigour and hope. The health of men at work is the challenge which confronts us to-day; and how we meet this challenge concerns not only our own people but all humanity.

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THE TOXICITY OF EPICHLORHYDRIN VAPOUR

BY

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A versatile apparatus is described for exposing experimental animals to predetermined concentrations of toxic substances in air, and it has been used to study the vapour toxicity of epichlorhydrin to rats and rabbits. At concentrations above 100 p.p.m. the vapour produces lung oedema and damage to the renal cortical tubules in rats, while above 50 p.p.m. it produces marked nasal irritation. Nasal irritation is still present in rats and rabbits below 50 p.p.m. and is only absent below 10 p.p.m. It is recommended that the concentration in industrial atmospheres should not exceed 5 p.p.m.

Epichlorhydrin is a colourless liquid with a chloroform-like odour; its boiling point is 116° C., density 1·18 at 20° C. and vapour pressure 13 mm. at 20° C. It has the following structure

and its high chemical reactivity is due both to the epoxy group and to the chlorine atom. It is used as a stabilizer in certain chlorine-containing substances such as pesticides and chlorinated rubber and as an intermediate in many manufactures. Epichlorhydrin is finding an increasing outlet in the production of epoxy resins for surface coatings, castings, laminates, and adhesives.

There is not an extensive literature on the toxicity of epichlorhydrin, although some reference is made in the literature of one manufacturer to an experimental investigation (Freuder and Leake, 1941) which states that the liquid is a vesicant and a dermatitic agent to the skin, and that the vapour is irritating to the eyes, nose, and throat. It has been shown that the exposure of rats to an atmospheric concentration of 250 p.p.m. for four hours is lethal (Carpenter, Smyth, and Pozzani, 1949), but no maximal allowable concentration is recommended in any available published list. The present investigation was undertaken to ascertain the threshold of the toxic action of epichlorhydrin vapour on experimental animals, so that a limiting concentration for industrial atmospheres might be assessed.

Design of Exposure Chamber

The chamber in which the animals were exposed to test epichlorhydrin atmospheres is shown in Figs. 1 and 2. The animals were housed in the "perspex" exposure chamber, *A*, which stood in an outer glass-walled chamber, *B*, maintained at a slightly reduced pressure by means of an exhaust fan. The test atmosphere was led into the bottom of the exposure chamber through the glass column, *D*, and left the chamber through a series of holes near the base.

Generation of Test Atmospheres.—The epichlorhydrin atmospheres were prepared by atomizing solutions of epichlorhydrin in propanol into a metered stream of air by means of a controlled fluid-feed atomizer (Gage, 1953). This is shown at *C* in Fig. 2 and differs from the model previously described in having the atomizer fused directly to the glass syringe to prevent leakage. The piston of the syringe was lubricated with a glycerol-dextrin-mannitol grease (Meloche and Fredrick, 1932), which has been found to be much less readily attacked by organic solvents than other available lubricants. The atomizer assembly was clamped vertically with its tip penetrating a central hole in the sponge rubber seating *E* of the glass column *D*. The syringe was driven by a slow injection apparatus *F* (C. F. Palmer, Ltd.) which has been modified by the makers to be suitable for a vertical drive. This mechanism operates a ram by means of a synchronous motor through a set of gears which can drive the syringe piston at speeds of one inch in 10, 20, 40, 80, 160, or 320 minutes. The air supply to the atomizer was controlled by the valves *G*, *H*, and with a pressure gauge, *I*, shown on the right of the instrument panel in Fig. 1 and also displayed diagrammatically on the right of Fig. 3. A common compressed air-line for a block of three exposure chambers, controlled by a "nullmatic" pressure regulator (Sunvic Controls, Ltd.) brought air at a constant pressure of 15 lb. per square inch to valve *G* and thence to the needle valve *H*.

From *H* the air passed to the atomizer *C*, with a tee-piece for the pressure gauge *I*. At least once a week the calibration of the pressure gauge in terms of air-flow rate

FIG. 1.—Front view of exposure chamber.

FIG. 2.—Diagrammatic side view of exposure chamber shown in Fig. 1.

FIG. 3.—Diagrammatic arrangement of instrument panel of exposure chamber (not to scale).

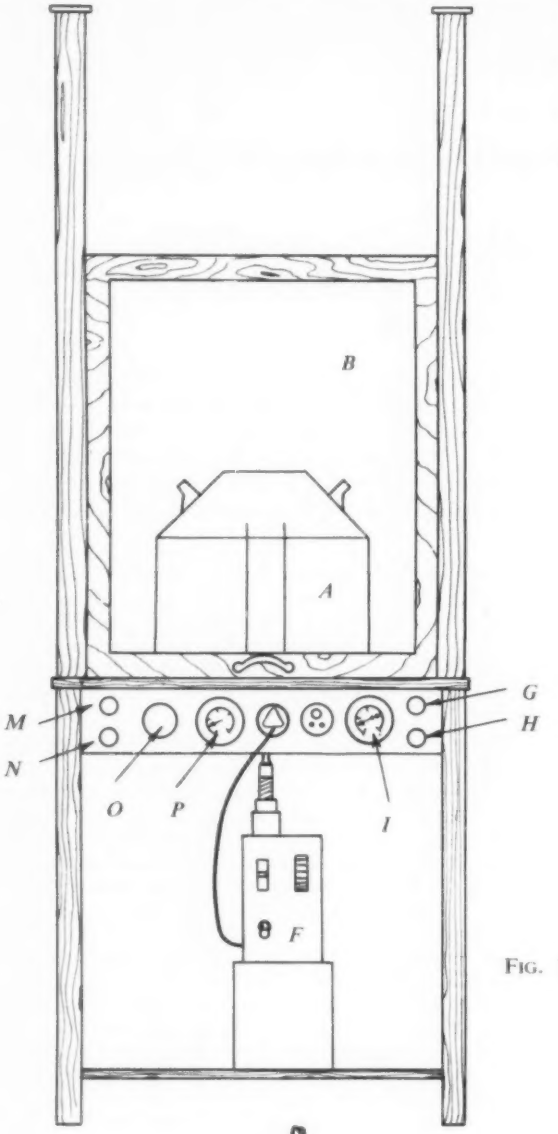


FIG. 1

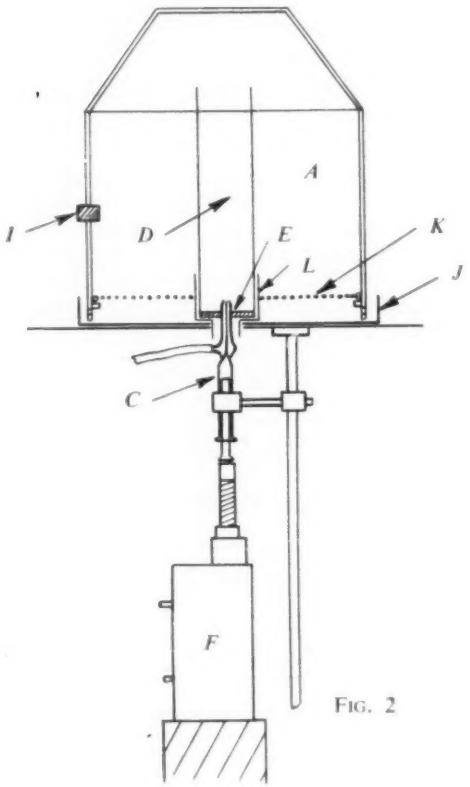
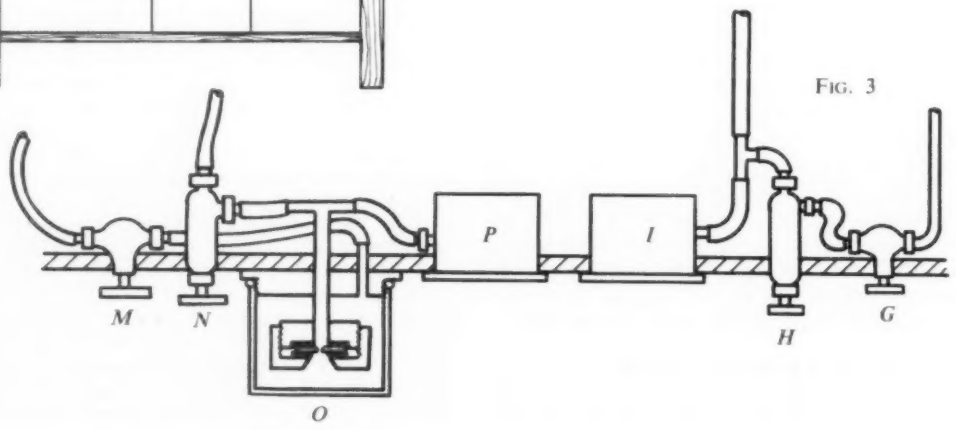


FIG. 2

FIG. 3



was checked by attaching a rotameter to the outlet of the atomizer. This system of flow control by needle valve and pressure gauge with a constant air-line pressure has been found to be simpler and at least as satisfactory as an individual pressure reducing valve and flow meter on each exposure chamber. The concentration of epichlorhydrin in the test atmosphere was calculated from the internal diameter of the syringe, the rate of movement of the piston, the concentration of epichlorhydrin in solution, and the air flow supplied to the atomizer.

Exposure Chamber.—The exposure chamber *A* was constructed from four perspex walls, 47 × 47 × 30 cm. high, with a detachable lid. The open bottom rested on an aluminium tray, *J*, and the animals were placed on a grid *K* constructed from stainless steel wire. The upper end of an aluminium collar *L*, which had a diameter large enough to take the glass column *D*, passed through a hole in the centre of grid *K*, and the narrower lower end passed through a smaller hole in the tray *J* and through another in the aluminium base of the outer chamber *B*. The glass column *D* was sealed into *L* by means of a sponge rubber pad *E*, which also carried a hole through which passed the tip of the atomizer *C*. The animals in the chamber were kept apart by means of radial partitions, eight of which were inserted on stainless steel supports round the centre glass column, and a second stainless steel grid was placed on top of these partitions to prevent the animals from climbing over them.

Analysis of Test Atmosphere.—A daily analytical check on the concentration of the epichlorhydrin atmospheres was made by the method described by Daniel and Gage (1956). For this purpose a sampling port was provided in the side of the exposure chamber, kept closed when not in use by means of a rubber stopper. The apparatus for drawing the required air sample through the absorber is shown on the left of Figs. 1 and 3. The sample of the test atmosphere was collected by means of a vacuum line controlled by a critical orifice plate; this provides a sampling rate independent of variations in the vacuum line and determined by the line pressure between the orifice and the absorber. The orifice plate can be seen at *O* in Fig. 3, screwed in its holder between two rubber gaskets; for sampling speeds of 0·5 to 1·0 l./min. an orifice with a diameter of 0·45 mm., flared on the upstream side to prevent turbulence, is suitable. A vacuum line was led to the orifice through the valve *M* and applied a vacuum of about 50 mm. mercury to the orifice. Between the sampling equipment and the orifice plate at *O* was the needle valve *N* and vacuum gauge *P*. The vacuum gauge was calibrated in terms of flow rate by replacing the sampling equipment with a suitable rotameter and taking readings of the rotameter and vacuum gauge over a range of settings of the needle valve. A check on this calibration was made at least once a week.

Experimental Results on Rats

At each test epichlorhydrin concentration four male and four female albino Wistar rats, within the weight range 160-200 g., were exposed to the atmospheres for daily six-hour periods, for five days a week. They were weighed daily and blood samples were taken weekly from the tail vein for haemoglobin determination by the Haldane method and for red and white cell counts and a differential white cell count on a Leishman-stained smear. Each week an 18-hour overnight sample of pooled urine from the female rats was taken for protein estimation by a colorimetric biuret method after trichloroacetic acid precipitation.

Eleven Exposures at 120 p.p.m.—After three hours of the first exposure all rats showed laboured breathing which remained throughout the subsequent exposure periods. Between the exposures they were lethargic and in progressively poor condition. After the fourth exposure a profuse nasal discharge developed. The rats showed a considerable loss in weight during the exposure and there was a marked leucocytosis due to an increase in both polymorphs and monocytes. At the termination of the exposures the urinary protein excretion was more than double the normal value. One rat died after the eleventh exposure.

At necropsy all lungs showed patches of discoloration, two livers had uneven coloration, and in two rats the kidney cortex was unusually pale. The intestines contained bile and were distended with gas. At histopathological examination the lungs of all rats showed congestion, oedema, consolidation, and areas of inflammation with signs of abscess formation. There was general congestion of the liver, in one case accompanied by areas of necrosis. The kidneys of all rats showed areas of leucocytic reaction and in four there was atrophy of the peripheral cortical tubules.

Eighteen Exposures at 56 p.p.m.—After the tenth exposure the rats appeared to be lethargic with some respiratory distress; later a nasal discharge appeared. The rats lost weight during the exposure days but recovered to some extent during the week-ends. The urinary protein excretion, haemoglobin, and red, white, and differential cell counts were within normal limits. No abnormalities were observed at necropsy or on histopathological examination, apart from abscess formation in one lung which was probably not attributable to the exposure.

Eighteen Exposures at 27 p.p.m.—Signs of mild nasal irritation were produced by this concentration, and the body weight remained constant during the exposure period. The lung of one rat at histopathological examination showed areas of haemorrhage and consolidation.

Nineteen Exposures at 17 p.p.m.—This group of rats gained weight normally though their condition

appeared somewhat inferior to that normal for this colony. Nothing abnormal was observed at necropsy or at histopathological examination.

Eighteen Exposures at 9 p.p.m.—Apart from two rats in this group which developed a pulmonary infection, the rats grew normally and appeared in good condition.

Experimental Results on Rabbits

The effect of lower epichlorhydrin concentrations has been tested on New Zealand white male rabbits within the weight range 1·8 to 2 kg. Two rabbits, exposed to 35 p.p.m. for 20 daily periods, showed signs of nasal irritation but increased in weight normally. Two more rabbits were exposed to 16 p.p.m. and also showed nasal irritation after two exposures; the concentration was decreased to 9 p.p.m. and then continued for 20 days without producing effects on the rabbits. Post-mortem and histopathological examination of these rabbits at the end of the exposure period showed no signs of any tissue changes which could be attributed to the exposures.

Discussion

A wide variety of exposure chambers are described in the literature, but the design used in this investigation has novel features which have been evolved during experience over a number of years. The "perspex" chamber gives complete visibility and is easy to clean and the outer casing prevents contamination of the laboratory atmosphere. This type of construction is less expensive and easier to operate than a sealed metal and glass chamber. The procedure for generating the test atmosphere has certain advantages over the more usual methods of bubbling the air through a volatile liquid, or metering the liquid on to a hot surface in an air stream. By the method described known concentrations can be prepared without knowledge of the physical constants of the substance and these concentrations can be varied at will, and impure samples or mixtures can be examined without a progressive change in the atmosphere during the experiment. The substance is completely volatilized into the air stream without the application of heat and the bulk is not exposed to continuous aeration with the attendant possibility of oxidation, polymerization, or other chemical changes. If a solution of a non-volatile liquid or solid in an inert volatile solvent is used in the syringe, a fine mist or dust is produced, and low dilutions of a gas can be prepared by directly injecting the gas into the air stream by means of a large glass syringe.

The results obtained with epichlorhydrin vapour on rats indicate that above 50 p.p.m. it produces a marked nasal irritation, and above 100 p.p.m. it can give rise to pulmonary oedema together with damage to the renal cortical tubules. There can be little doubt that this toxic effect is due to the chemical action of the epoxide group which is rendered more active by the presence of the chlorine atom, as epichlorhydrin is much more toxic than ethylene oxide and propylene oxide (Hollingsworth, Rowe, Oyen, McCollister, and Spencer, 1956). It is well known that the epoxide ring can react with anions to form esters and it seems probable that modification of cell proteins by esterification of carboxyl groups gives rise to a change in function which recalls the effects produced by phosgene and ketene, which have been attributed to the acetylating action of these substances on tissue proteins (Potts, Simon, and Gerard, 1949).

The experiments on rats and rabbits have shown that nasal irritation is still apparent below 50 p.p.m. epichlorhydrin and under the experimental conditions is only absent below 10 p.p.m. In the rat experiments there was some evidence of a higher incidence of lung infections than is encountered when rats of this colony are maintained in the exposure chamber, and although this may be fortuitous, the possibility that the inhalation of the vapour can predispose to infection should not be ignored. It is recommended that the concentration of epichlorhydrin in the atmosphere where men are continually working should not exceed 5 p.p.m. unless respiratory protection is used. This concentration can readily be determined in air (Daniel and Gage, 1956).

Technical assistance in this investigation was supplied by Mr. Z. S. Bérczy, and I am indebted to Dr. J. G. S. Crabbe for a pathological report on the histological preparations. The exposure chambers were constructed by the Engineering Department of the I.C.I. Akers Research Laboratories.

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THE RESPONSE TO HEINZ BODIES IN THE RAT

BY

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Irregular refractile granules which occur within red blood cells were first described by Heinz in 1890. The precise nature of these bodies is unknown. The present work was undertaken in order to help to assess the significance of the presence of Heinz bodies in the blood over a considerable period.

Heinz bodies have been produced in the red blood cells of intact and splenectomized rats over relatively long periods by continuous feeding of azo geranine. The proportion of Heinz-body red blood cells quickly rose to a peak and then fell to fluctuating lower values; there was a concurrent fall in the red blood cell count and reticulocytosis. There were more Heinz-body red blood cells and a greater fall in the red blood cell count in the splenectomized animals. Large deposits of haemosiderin were present in the livers of the splenectomized animals fed the dye. Little or no haemosiderin was found in the livers of intact animals fed the dye or in those of splenectomized animals not receiving dye. Splenic hyperplasia accompanied the initial increase in Heinz-body red blood cells and remained undiminished after the level had fallen. The half-time survival of Heinz-body red blood cells transfused into normal rats was approximately one day compared with over five days in splenectomized animals. The anaemia associated with the appearance of Heinz bodies was found to be hypochromic: the mean cell haemoglobin concentration fell from 35·7% before feeding dye to 26·7% at the time of peak Heinz-body red blood cell concentration after seven days of dye feeding. With the subsequent fall in Heinz-body red blood cell level, approximately half of the deficiency in the mean cell haemoglobin concentration was replaced, despite a substantial recovery in the packed cell volume without an increase in the red cell count. Twenty days after feeding the dye had been stopped, no Heinz-body red blood cells were found, and all values had returned to normal.

The irregular refractile granules which occur within red blood cells and may measure up to 3 μ in diameter were first described in detail by Heinz (1890). The precise nature of the material of Heinz bodies remains undecided, but the bulk of recent evidence, which has been reviewed by Fertman and Fertman (1955), indicates that they are composed of haemoglobin degradation products. Heinz induced these granules by administering phenyl hydrazine to animals, and since that time Heinz bodies have been primarily associated with the presence of foreign substances in the blood, notably aromatic amines and aromatic nitro compounds. However, it is clear that endogenous factors also cause Heinz bodies, for these inclusions are found normally in the cat (Hecht and Wingler, 1952), and in small numbers after splenectomy in the human subject (Zadek and Burg, 1930; Selwyn, 1955) and in the rat (Sorina, 1937; Rofe, 1957, unpublished). In the latter observation only some animals were affected, and in these a few Heinz bodies were seen during the first six weeks, but not later. The occurrence of Heinz bodies in the newborn human is also reported (Varadi and Hurworth, 1957).

The present work was undertaken to help to assess the significance of the presence of Heinz bodies in the blood over a relatively long period of time. A Heinz-body-forming substance has been administered continuously in the diet and the incidence of affected red cells and concurrent changes have been observed in intact and in splenectomized rats.

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Methods

Proportions of Heinz-body Red Cells and Reticulocytes and R.B.C. Count during Chronic Induction of Heinz Bodies in Intact and Splenectomized Rats.—Fifteen male rats weighing 250-300 g. were used. Seven of these were splenectomized: anaemia due to Bartonella infection developed within a week or two, but on examination four months later, normal numbers of red cells and reticulocytes were found. Heinz bodies were absent. Four splenectomized rats and four intact rats were given the Heinz-body-producing dye azo geranine* in the diet at a concentration of 1·5% w/w for 73 days, and the remaining rats (three splenectomized and four intact) were used as controls receiving the same diet but without dye. Tail blood from all animals was examined from time to time during this period and afterwards as follows: The incidence of Heinz-body red blood cells (H.B.R.B.C.s) was found by counting at least 500 cells stained supravitally with methyl violet: one drop of stain (half saturated in normal saline containing 0·2% citrate) on a slide, was mixed with one quarter this volume of blood on a coverslip. The R.B.C. count was made in duplicate on a sample diluted with formalin citrate (Dacie, 1956) in a red cell pipette. The same pipette was used for a given animal, and the same counting chamber (improved Neubauer ruling) was used for all. The incidence of reticulocytes was determined in at least 500 R.B.C.s smeared after supravital staining with brilliant cresyl blue (Dacie, 1956).

In order to obtain an indication of the condition of the spleens and livers of the above animals at the end of the dye-feeding period, six intact rats and six rats splenectomized for four months were killed after completing the same course of dye feeding. As a control for any liver changes which might appear solely as a result of splenectomy, five rats from which the spleens had been removed several months previously and which had not had dye were killed also. Formol-fixed sections of all the spleens and livers were treated with HCl and $K_4Fe(CN)_6$ to show the presence of haemosiderin and then stained with safranin; further sections were stained with haematoxylin and eosin.

Weight of Spleen during Chronic Heinz Body Induction.—Twenty-six male rats on a diet containing azo geranine (1·5% w/w) were killed in unselected groups of four at various times up to 43 days after the beginning of ingestion of the dye; the two animals remaining after this time were returned to a normal diet for seven days before being killed. All animals were killed by ether and were not bled: the body weights and spleen weights were then determined without delay. Eight control rats which had not had dye were treated in the same way, four being killed before and four after the course of feeding dye to allow for the intervening period of growth.

Survival of Transfused Heinz Body Blood.—In four normal male rats and three male rats splenectomized four months earlier, about one-third of the blood volume was exchanged for blood of which 90% of the cells contained Heinz bodies. The donor rats had received azo geranine (1·5% w/w) in the diet for six days. Blood was taken by cardiac puncture and the pooled samples stored overnight in acid citrate dextrose solution (Dacie, 1950). The recipient rats were bled and transfused via the caudal vessels. The replacement of normal blood by an approximately equal volume of Heinz-body blood gave a final incidence of H.B.R.B.C.s of about 30%. The numbers in each animal were then determined from time to time until they fell below 1%.

Proportion of H.B.R.B.C.s, R.B.C. Count, Packed Cell Volume, and Haemoglobin Concentration.—Ten female rats were given azo geranine in their food at a concentration of 1·5% (w/w) for 85 days. Before, during, and after this period, on a total of nine occasions, determinations were made, as follows, on tail blood taken from these rats and from nine control animals.

The proportion of H.B.R.B.C.s was found as described above. The R.B.C. count was made on a 0·02 ml. sample taken with a British Standard (B.S.) 0·02 ml. haemoglobin pipette and diluted to 4 ml. with formalin citrate (Dacie, 1956). The same individual haemocytometer chamber (improved Neubauer ruling) was used throughout the experiment for all samples: the cells on 80 small squares were counted and the mean of the counts of duplicate samples was taken. The packed cell volume (P.C.V.) was determined by centrifuging a column of blood approximately 10 cm. long in a heparinized capillary tube for 30 min. at 3,000 rev./min. on a maximum radius of 17 cm. The length of the red cell column was then expressed as a percentage of the whole; the mean of duplicate values was corrected for trapped plasma, using the factor for rat blood (0·96) supplied by Huang and Bondurant (1956). Haemoglobin was estimated by the method of Haldane (100% standard = 14·8 g./100 ml.). British Standard 0·02 ml. pipettes and dilution tubes were used throughout the experiment. The mean of duplicate determinations was taken. When Heinz bodies were present their release on haemolysis caused cloudiness in the haemoglobin solution. It was therefore necessary to haemolyse the blood sample in a small, sharply-pointed centrifuge tube and after spinning for 15 min. at 3,500 rev./min. the supernatant was transferred, without loss, to the usual comparator dilution tube: this procedure was carried out on blood samples from both the control and the experimental animals when Heinz bodies were present in the latter. It was also found that after passing coal gas through the centrifuged haemoglobin solution deriving from Heinz-body blood, a faint brownish hue was discernible which was not in the control blood after identical treatment. This difference was very slight, but lest it should jeopardize the accuracy of matching in the comparator, a second pair of blood samples from each animal was estimated by the cyanmethaemoglobin method (Dacie, 1956). (The standard used was a sample of normal rat blood on which 12 determinations had been carried out by two observers, using the Haldane method.) The values obtained by this modification were close to those obtained by using the comparator, and showed no consistent difference; the results were therefore pooled,

*Disodium salt of 8-acetamido-2-benzeneazo-1-naphthol-3:6 disulphonic acid.

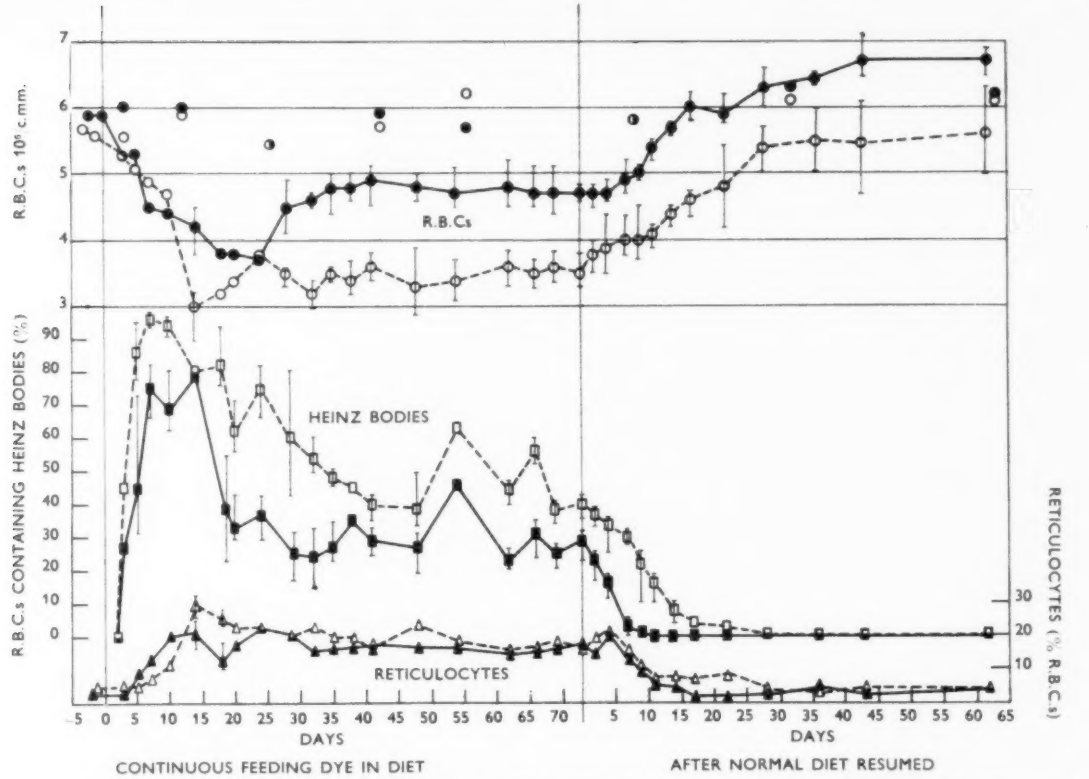

FIG. 1.—The R.B.C. count and the incidence of Heinz-body red cells and of reticulocytes in intact ●—●, ■—■, ▲—▲, and splenectomized ○—○, □—□, △—△, rats given azo geranine in the diet. The points which are not joined represent R.B.C. counts of the control rats, intact: ●, and splenectomized: ○, which received no dye. The ranges are given as vertical lines where this is possible without overlap.

and the mean of the 40 individual determinations on the 10 experimental rats was taken as the value for the group.

Results

Proportion of Heinz-body Red Cells and Reticulocytes and R.B.C. Count during Chronic Induction of Heinz Bodies in Intact and Splenectomized rats.—Figure 1 shows the changes observed. The incidence of H.B.R.B.C.s in intact rats during the course of chronic dye ingestion followed the pattern described earlier (Rofe, 1957) for other Heinz-body-producing azo dyes. This consists of a latent period, a relatively rapid rise to a peak concentration, and a slower fall to a fluctuating lower level, which is maintained so long as the dye is given. In the splenectomized animals the H.B.R.B.C.s level rises more rapidly and to a higher peak than in the intact animals; it falls more slowly and remains higher throughout the experiment. When a normal diet is resumed the intact animals remove all Heinz bodies from the circulating blood in nine days, but in the absence of the spleen this takes as long as 25 days.

Figure 1 also shows the development of anaemia and corresponding reticulocytosis. The maximum anaemia occurs in both groups some days after they reach peak H.B.R.B.C. values; during the following two weeks recovery in the intact animals is considerable but not in the splenectomized animals, and thereafter the two levels of anaemia are maintained throughout the period of feeding the dye. On returning to a normal diet, recovery proceeds at about the same rate in each group, but on reaching their pre-dosage values the intact animals show a further increase and finally establish the same difference in red cell count compared with the splenectomized group that existed during the anaemic period. The control animals, intact and splenectomized, which were not given the dye, showed no significant trend.

Of the group which were killed at the end of the dye-feeding period, the intact animals were found to have greatly enlarged spleens (see overleaf), the increase being principally in the red pulp. Microscopic examination did not indicate an increase in

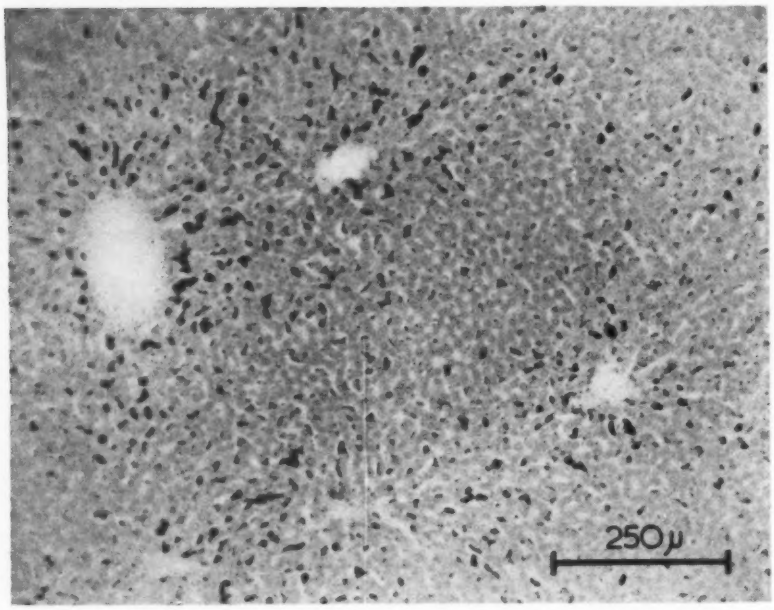

FIG. 2.—Section showing haemosiderin in the liver of a splenectomized rat after chronic induction of Heinz bodies by azo geranine. Intact animals treated in the same way and chronically splenectomized animals not given the dye, showed little or no haemosiderin. Prussian blue reaction followed by safranin.

the concentration of haemosiderin although of course the absolute amount was greatly augmented. The livers of these rats had a normal structure and contained very little haemosiderin; the livers of the splenectomized dye-fed rats, on the other hand, contained large amounts of haemosiderin (Fig. 2) but were otherwise normal. The livers of splenectomized rats which had not had dye showed little or no haemosiderin.

Spleen Weight during Chronic Heinz-body Induction.—Between the third and the fifth day of feeding the dye the average ratio of the spleen weight to the body weight of the unselected groups of four animals killed increased to more than three times the average value of the normal animals (Fig. 3). This increase began after the appearance of Heinz bodies, for on the third day, when spleen weights were normal in the animals killed, Heinz bodies were already present in 11% of their erythrocytes. The maintenance of undiminished hyperplasia is evident from the final values obtained after 43 days of Heinz-body induction (Fig. 3). The time taken to return to normal in the two remaining animals was closely similar to that taken to eliminate Heinz bodies in the experiment of Fig. 1.

Survival of Transfused Heinz-body Blood.—When approximately one-third of the blood volume was replaced by blood in which 90% of the erythrocytes contained Heinz bodies, normal rats showed virtually no Heinz bodies after four days. By contrast, the same initial proportion of Heinz bodies took 15 days to disappear from splenectomized rats. Fig. 4 shows the mean levels of surviving H.B.R.B.C.s at different times, expressed as a percentage of the initial levels determined shortly after the blood exchange.

Proportion of Heinz-body Red Blood Cells, Red Cell Count, Packed Cell Volume, and Haemoglobin Concentration.—In order to show the relative sizes of the changes which occurred, the different factors have been plotted in Fig. 5 as percentages of the respective mean values found on two occasions before feeding dye to the experimental group of animals was started.

It will be seen that after eight days, when 95% of the red cells contained Heinz bodies, the R.B.C. count was reduced by one third; a corresponding fall occurred in the P.C.V. but the haemoglobin concentration fell further, to little more than half of its original value.

Some five weeks later, despite the undiminished intake of dye, two-thirds of the R.B.C.s were free of Heinz bodies and considerable recovery had taken place in both the P.C.V. and the haemoglobin concentration: only the R.B.C. count remained unchanged. Slight increases in all values were found after a further six weeks, when the administration of azo geranine was stopped. Three weeks later the red cell count had returned to normal and the haemoglobin value had risen correspondingly.

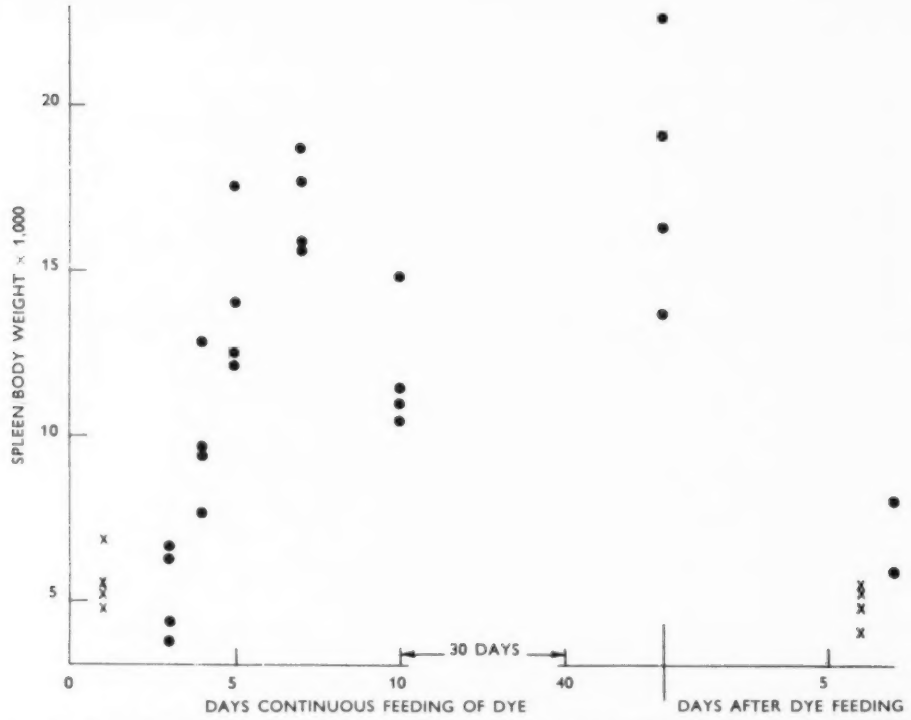

FIG. 3.—Splenic hyperplasia in rats during chronic feeding of the Heinz-body-inducing dye azo geranine: each point represents the spleen/body weight ratio of an individual animal. The values for each of eight control animals are shown marked thus ×.

A smaller increase in the P.C.V. brought this value into the normal range also. During the next 18 weeks further determinations showed no significant differences from the control group.

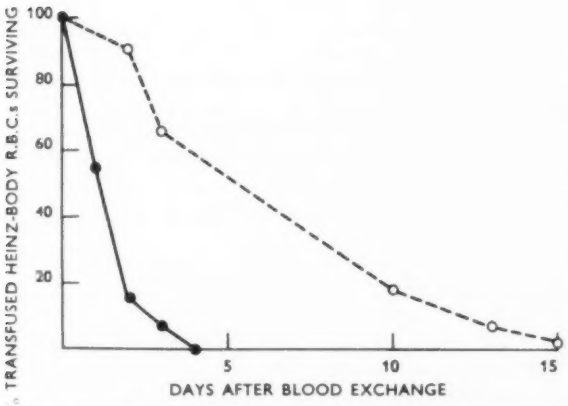

FIG. 4.—The survival of transfused Heinz-body red cells in normal, ●—●, and splenectomized, ○—○, rats. The incidence of Heinz-body red cells one hour after transfusion was taken as 100% survival.

Discussion

That the splenomegaly and anaemia are the response to the presence of Heinz bodies in the erythrocytes and are not due to the direct action of the dye seems probable from the following evidence. In the intact animals (Fig. 1) the anaemia varies according to the level of H.B.R.B.C.s and is not constant as is the dye intake; similarly, the splenic enlargement does not begin until after Heinz bodies are present in substantial numbers. Other dyes of very similar structure (yellow FCS, Ponceau RS, lissamine) which do not produce Heinz bodies, do not produce anaemia or splenomegaly when administered in the same molecular amounts under the same conditions.

The constancy of the daily rate of ingestion of the dye and its rapid excretion (Daniel, 1958, personal communication) provide what may be thought of as constant Heinz-body inducing conditions.

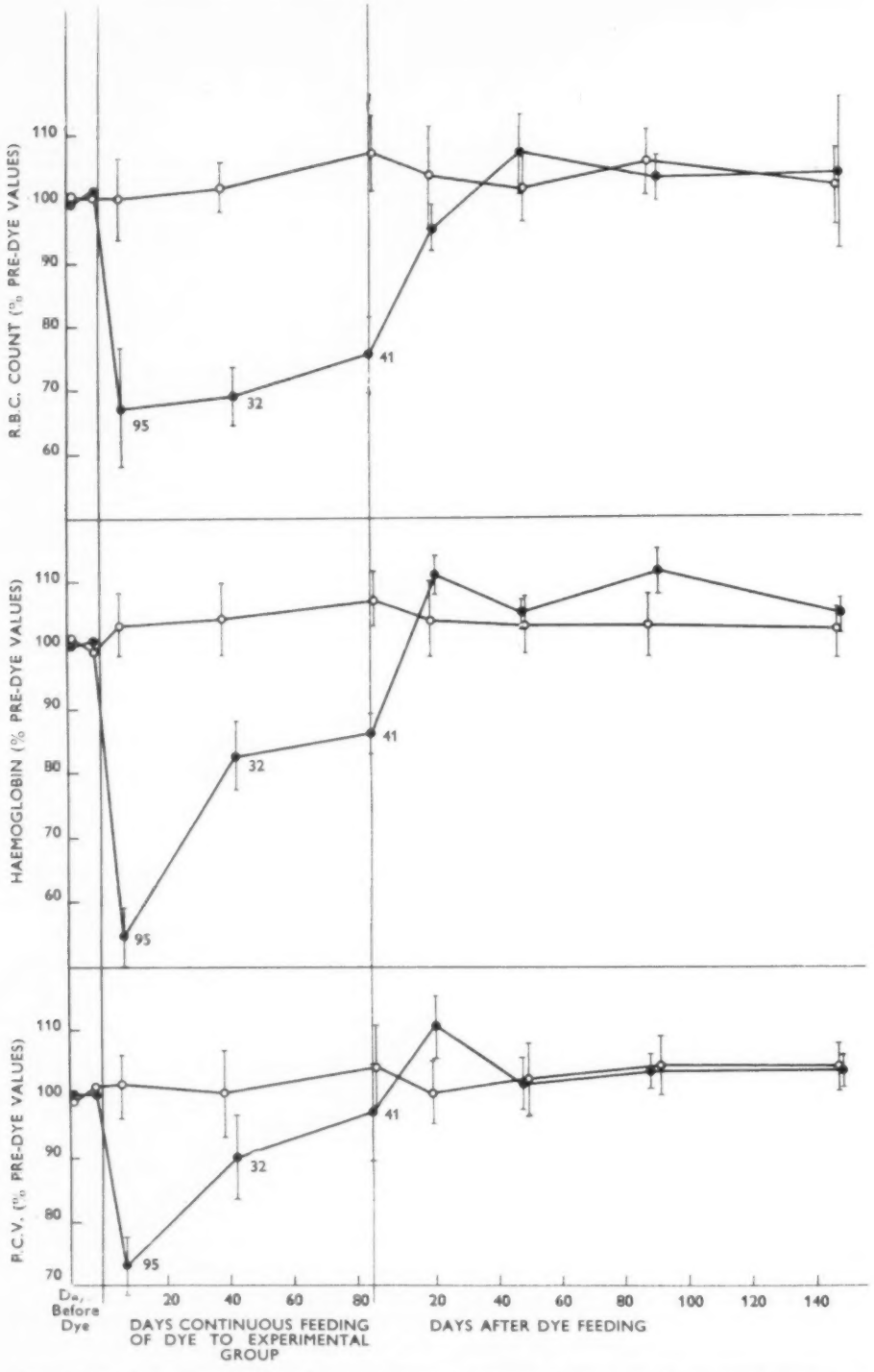

FIG. 5.—The relative changes in red cell count, haemoglobin concentration, and packed cell volume in Heinz-body anaemia. Control group of nine rats (no dye feeding) ○—○, experimental group of 10 rats ●—● received azo geranine. Vertical lines represent ± standard deviation. All values are directly comparable since they are expressed as percentages of the respective levels prevailing before feeding of dye to the experimental group began: these levels were as follows. R.B.C. count (10^6/c. mm.): control, 5·6; experimental, 5·6. Haemoglobin concentration (g./100 ml.): control, 15·5; experimental, 15·3. Packed cell volume (corrected for trapped plasma): control, 43·1%; experimental 42·9%.

The numbers adjacent to some points refer to the concurrent percentage of H.B.R.B.C.s; at all other points no H.B.R.B.C.s were present.

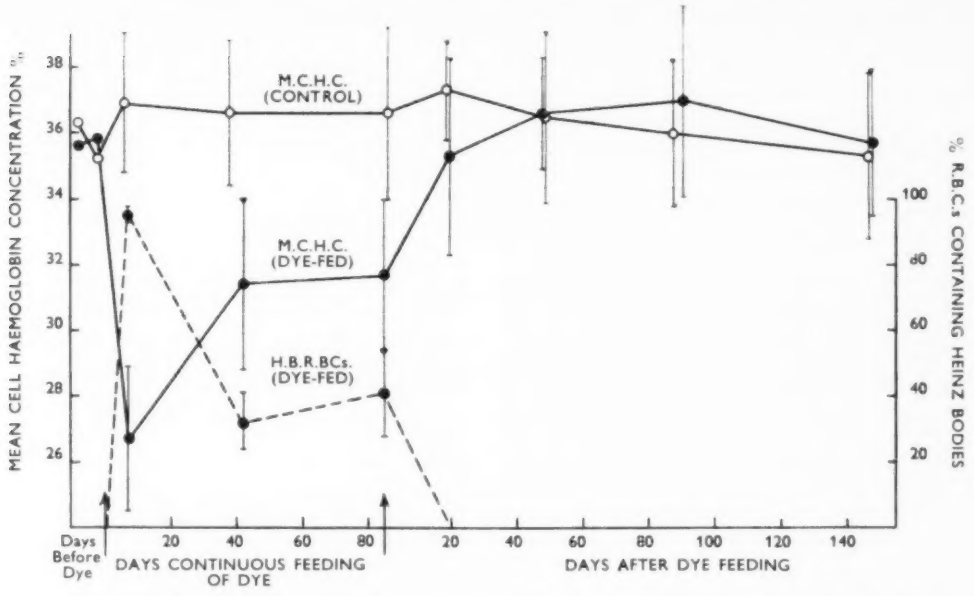

FIG. 6.—The mean cell haemoglobin concentration in nine control rats, ○—○, and in 10 rats in which Heinz bodies were induced by feeding azo geranine, ●—●. Vertical lines show ± the standard deviation.

Thus, if Heinz bodies are tending to be produced in the red cells at the same rate throughout the experiment, the observed fluctuation in their concentration (Fig. 1, intact animals)—the initial rapid rise, the brief period of high concentration, and the fall to a maintained lower level—indicate varying activity of the factors opposing an increase of Heinz bodies. At first the major factor is the removal of the affected erythrocytes from the circulating blood. This is shown by the pronounced increase in the size of the spleen and haemosiderin deposition, and the rapidly developing anaemia. Subsequently, there appears to be an increase in haemopoietic activity, for considerable recovery from the anaemia occurs despite the continued high level of blood destruction which the maintained splenomegaly (Fig. 3) presumably indicates. The mechanism, by which the H.B.R.B.C. concentration is reduced and kept at a lower level despite the unchanged conditions, thus appears to depend upon an increased turnover of red cells.

An indication of the part played by the spleen in the response to Heinz bodies is given by comparing the values for intact and splenectomized rats in Fig. 1. The absence of the spleen appears to impair the ability to remove red cells containing Heinz bodies, but the differences observed in this respect between the intact and the splenectomized cannot show the full extent of the contribution of the spleen, since in the splenectomized rats the red cell destroying function of the liver is greatly increased, as is shown by the extensive deposits of haemosiderin, which are almost absent in the intact animals and in splenectomized animals not receiving the dye. Confirmation of the importance of the spleen in the removal of H.B.R.B.C.s is given by the transfusion experiment (Fig. 4). The half-time survival of H.B.R.B.C.s (taking the numbers an hour after transfusion as 100%) in intact rats is seen to be approximately one day, whereas in splenectomized rats it is five and a half days. This value approaches that reported for normal red cells in normal rats (Hall, Nash, and Hall, 1957). These authors injected Cr^{51}-tagged red cells into normal rats, and taking the value found one hour later as 100%, obtained a half-time survival of about eight days. It thus appears that loss of the spleen results in loss of much of the ability to discriminate H.B.R.B.C.s, which are treated more as though they were normal red cells.

The greater degree of anaemia which is seen in the splenectomized animals (Fig. 1) is surprising in view of the reduced ability to destroy red cells (Fig. 4). The explanation of the partial recovery which occurs in the intact animals may perhaps lie in the development of haemopoietic function by the spleen: this has been reported in Heinz-body anaemia in rabbits (Treon, Deichmann, Sigmon, Wright, Witherup, Heyroth, Kitzmiller, and Keenan, 1949). On the other hand, Pirrie (1952), who produced chronic

red cell stippling in guinea-pigs by daily administration of lead nitrate, found that the associated anaemia was less in splenectomized animals, and the proportion of stippled cells was higher.

Under the conditions of the present study Heinz bodies were usually found singly in the red cell and occupied about a third to a fifth of the cell diameter: they may thus be expected to represent an appreciable quantity of haemoglobin lost to the cell. That Heinz-body anaemia is markedly hypochromic is shown in Fig. 6 where the average values for mean cell haemoglobin concentration (M.C.H.C.) are shown. It will be seen that a reduction in the initial high concentration of H.B.R.B.C.s was associated with an increase of the M.C.H.C.; when six weeks later no significant change in the concentration of H.B.R.B.C.s had occurred, there had likewise been no change in the M.C.H.C.; finally, the elimination of H.B.R.B.C.s was accompanied by a rapid recovery of the normal M.C.H.C. It will also be noted that the first increase in M.C.H.C. took place despite the concurrent increase in cell size which is indicated by the increase in packed cell volume without change in the red cell count (Fig. 5).

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TOXIC SOLVENTS: A REVIEW

BY

ETHEL BROWNING

The literature on toxic solvents increases in volume from year to year, almost from day to day, both concerning those already known and closely investigated by a multitude of observers and also those new chemical compounds constantly being introduced in industrial processes.

One of the most striking features of recent developments has been the extension of knowledge afforded by new and sometimes very complex scientific methods of examining the physiological response, metabolic processes, and detoxication mechanisms of animals and human beings subjected to the toxic effects of certain solvents; the detection and identification of their presence in mixtures; the chemical relationship of members of the different groups; and the measurement of the concentrations of their vapour in the atmosphere of workrooms. With regard to new solvents which have been produced in recent years, it is fortunate that the majority of them, investigated by modern methods, have proved on the whole less hazardous, particularly from the viewpoint of chronic systemic poisoning, than some of the older substances whose toxicity was revealed by involuntary human experiment.

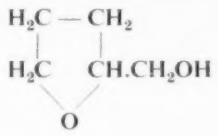
GENERAL DEVELOPMENTS

Experimental Physiology

Animal experiments, while undoubtedly useful in providing evidence of the nature and extent of the biological injury inflicted on living tissue by poisonous chemical substances, have certain disadvantages. Among these are the differences in response between animals and human beings and between different species of animals, due to some extent to differences in their metabolic processes; variations in the toxic effect of a compound according to its route of administration; and the fact that if the effects of long-continued exposures in conditions approximating to those of industrial exposure are to be accurately determined, the investigations must necessarily be prolonged and intricate.

The usual method of expressing the acute toxicity of a solvent is the L.D. 50, the dose in milligrams per kilogram of body weight which kills one half of the animals under investigation. Comparisons can be made of the toxicity relative to that of other solvents, and the variation in response according to the route of administration. This is exemplified in the following account of an experiment undertaken to determine the toxicity, and therefore the suitability of a solvent for toxicological test of various compounds (E. F. Edson, personal communication).

The solvent under examination was tetrahydrofurfuryl alcohol, a colourless liquid boiling at 178°C.



Administered intraperitoneally to rats its L.D. 50 was approximately 1,000 mg./kg., with no appreciable toxic effects at 500 mg./kg. Oral administration gave a similar type of toxic effect (weakness, narcosis, tachycardia, and urinary incontinence) occurring between 1,000 and 2,000 mg./kg., but the L.D. 50 by this route was 4,000 mg./kg., four times that of the intraperitoneal route, while the subcutaneous lethal dose was 2,000 mg./kg. From these estimates a comparison could be made with the toxicity of propylene glycol administered by similar methods. Propylene glycol proved to be the less toxic both orally and intraperitoneally, but the margin between the non-toxic and the lethal doses was less than with tetrahydrofurfuryl alcohol.

In determining acute toxicity by inhalation the L.C. 50 (the concentration of the gas or vapour that will kill one half of the animals in a given time), or the L.T. 50 (the time required to kill one half of the animals by a given concentration of the gas or vapour) is used (Gross, Schrenk, and Walmer, 1956).

Investigations of chronic toxicity by animal experiments are, however, long-term studies requiring two or more years, different species of animals, and detailed morphological examinations of organs and tissues.

An assessment of toxicity based on the L.D. 50 may differ considerably from that based on chronic exposure. This can be seen clearly if the classification of toxicity of some solvents given by Fairhall (1957)

on the former basis is translated into a corresponding classification estimated from the maximum allowable concentrations (or threshold limit values) published in 1958 by the American Conference of Governmental Industrial Hygienists. In Fairhall's classification, Class I is designated as " extremely toxic ", Class II as " very toxic ", Class III as " moderately toxic ", and Class IV as " slightly or nearly non-toxic ". In the threshold limit values, a level of 1 to 5 p.p.m. may be interpreted as corresponding to Class I, 5 to 100 p.p.m. as Class II, 100 to 500 p.p.m. as Class III, and 500 p.p.m. upwards as Class IV. The table illustrates the difference in classification of some solvents as estimated according to their acute or chronic toxicity.

Substance	Threshold Limit Value	L.D. 50 Value
Butyl alcohol	Class III	Class IV
Butylamine	Class I	Class III
1-chloronitropropane	Class II	Class I
Cresol (all isomers)	Class I	(p-cresol) Class IV
Diethyl sulphate	Class II	Class III
Dimethyl sulphate	Class I	Class IV
Dioxane	Class III	Class IV
Ethylenediamine	Class II	Class IV

The great improvements in the technique of inhalation experiments have been largely responsible for the development of one of the most useful guides to the control of health hazards at present available, namely, the annual publication already mentioned of the threshold limit values, or maximum allowable concentrations, of contaminants above which workers should not be exposed for an eight-hour working day. While these values are not offered as a " fine line " between safe and dangerous concentrations they do represent, based as they are on both industrial experience and also animal experimentation by observers in practically every country, a picture of the potentially hazardous environmental situation, and a comparison of the relative toxicity of a large number of solvents. Their number increases with every annual review, and in the light of new experience the values of some of those previously published are re-assessed and their levels altered either upwards or downwards in the light of the most recent evidence.

The most striking example of lowering of the threshold limit value during recent years is benzene, which has been reduced from 100 p.p.m. in 1926 and 35 p.p.m. in 1949 to 25 p.p.m. in 1957. This last reduction was based not on animal experiments but on the industrial experience of the death of a worker exposed to this level (Greenburg and Moskowitz, 1945). Other recent reductions are those of butyl cellosolve from 200 to 50 p.p.m. and carbon tetrachloride from 100 p.p.m. to 25 p.p.m. Among new compounds of relatively high toxicity added to the list during the last two years are decaborane (0·05 p.p.m.), furfural (5 p.p.m.), and isopropylamine (5 p.p.m.).

The Metabolism and Detoxication of Solvents

A feature of some interest on which the attention of many investigators has been focused in recent years is the metabolic transformation of various toxic substances within the body, and the relation of these metabolic products to their injurious effects on particular organs and tissues. These investigations are not in themselves of very recent development; the formation of conjugated sulphates during the metabolism of benzene was fully described by Yant, Schrenk, Sayers, Horvath, and Reinhart as early as 1936. Knowledge of these processes has, however, been greatly facilitated by the technical application of spectrophotometric methods, chromatography, and the use of radioactive tracers.

Spectrophotometric Methods. — Spectrophotometric determinations of certain halogenobenzenes (fluoro-, chloro-, bromo-, and iodo-benzene) have been described by Azouz, Parke, and Williams (1952), using the absorption spectra of these substances in ethanol and selecting suitable wave-lengths and extinction of absorption bands. By this method it was possible to compare the quantitative aspects of the metabolism of these substances with that of benzene itself.

Paper Chromatography.—This is a suitable method of estimating metabolites directly from body fluids. About 5 to 10 μg. of the fluid under investigation is placed in spots on a base drawn on the chromatographic paper, the lower edge of which is placed in contact with a composite solvent mixture consisting of one liquid which covers the paper (the stationary phase) and another which moves across it (the mobile phase). Each component of the spot flows in the mobile phase across the paper at a different speed. The position of the spot is determined, after removal of the solvent, by spraying the paper with a substance forming a coloured compound with the component. Each component is identified by the ratio of the distances from the base line travelled by the component and by the solvent.

Radioactive Tracers.—Quantitative measurements may be made by means of optical density, ultraviolet spectrophotometry, or using radioactive tracers. The technique of using radioactive tracers for identifying the nature, fate, and relative amount of excretion of metabolites of toxic substances (Popják, 1950) is well exemplified in the experiments on benzene described in detail by Parke and Williams (1953). They administered ^{14}C-labelled benzene by stomach tube, and the radioactivity of the

urine, the tissues, and the expired CO_2 was compared with that of known amounts of labelled benzene. It was thus found possible to estimate the amount of benzene eliminated in the expired air (about 45% in two days, of which 43% was unchanged and about 1·5% in the form of CO_2) and the amount eliminated in the urine (nearly 35%, consisting mainly of conjugated phenols), and to identify other urinary metabolites such as quinol, catechol, hydroxyquinol, and a small amount of phenyl-mercapturic acid. Nearly 80% of the dose of benzene was excreted in the expired air and urine in two to three days, while the remainder was eliminated slowly, about 5% remaining after this time in the tissues generally as metabolites of benzene.

Considerable light has also been thrown by this method on the metabolism of carbon tetrachloride (McCollister, Beamer, Atchison, and Spencer, 1951). It was found that about 50% of the CCl_4 absorbed was later eliminated in the expired air, and that although the blood concentration at the end of exposure to 46 p.p.m. was low, there were considerable amounts of radioactive carbon in the urine as an unidentifiable compound, possibly an organic chloride. As Elkins (1954) has remarked, if this substance could be identified and its separation from inorganic chlorides achieved, we might have a method of evaluating CCl_4 exposure by analysis of urine.

These investigations of the way in which the enzymatic processes of the body attempt to deal with toxic substances introduced from outside are being carried out with increasing frequency and scope, and their results provide an insight into the biological function of detoxication. Several industrial solvents have been examined by these methods and their ultimate fate in the body was described by Truhaut (1953b). A comprehensive table of end-products, in the form of urinary metabolites of a large number of substances, has been drawn up by L. J. Sciarini in Appendix II of Fairhall's " Industrial Toxicology ".

Such investigations have also gone far towards explaining the difference in toxicity of members of the same chemical group. The extreme toxicity of benzene to the haemopoietic organs following chronic exposure, contrasted with the relative non-toxicity in this respect of another aromatic hydrocarbon, cyclohexane, is due to the final metabolism of benzene to phenolic compounds, including pyrocatechol and hydroquinol, which are mitotic poisons with a special predilection for proliferating tissues such as the bone marrow; cyclohexane, on the other hand, is transformed first into cyclohexanone and finally into adipic acid, which has no special affinity for the haemopoietic tissues (Treon, Crutchfield, and Kitzmiller, 1943; Fabre, Truhaut, and Péron, 1952). Similarly, the higher toxicity of ethylene glycol compared with that of its group relative, propylene glycol, both used as solvents for cellulose varnishes, is explained by differences in their metabolism. Ethylene glycol is transformed first into glycollic acid, then into oxalic acid, which has an injurious effect on the kidneys, whereas propylene glycol gives rise only to a normal product of glucide metabolism, probably lactic acid, which is quite innocuous (Truhaut, 1953a). The formation of these harmless metabolites is regarded as a process of detoxication of which the principal site is believed to be the liver, with assistance from the endocrine glands, especially the thyroid and the adrenal cortex. In the transformation of trichloroethylene into trichloracetic acid, the lungs and spleen are also active in detoxication (Grandjean, Munchinger, Turrian, Haas, Knoepfel, and Rosenmund, 1955).

Estimations of Atmospheric Concentrations

Many methods have been used for estimating atmospheric concentrations of mixed contaminants, and though they have been developed to a high degree of accuracy, the separation of an individual constituent of a mixture, for example of aromatic hydrocarbons, is a tedious and time-consuming procedure. In general, colorimetric analysis is used for the determination of organic vapours by the formation of a coloured product which can be matched against a known standard. In most of such tests a measured volume of air is drawn through either a test paper or an impregnated silica gel. A description of this colorimetric method for the detection of 12 of the more common industrial contaminants was published in 1939 by the Department of Scientific and Industrial Research; this method is still in use, but it has a limited value for some of the solvents on account of its insufficient sensitivity for the levels now considered as the lower toxic limits. A method for the rapid determination of some aromatic hydrocarbons (benzene and its homologues) in air, by means of a stable direct-indicating gel utilizing a sulphuric-formaldehyde reagent, was described by Hubbard and Silverman in 1950. The qualitative colour differentiation was sensitive to benzene (reddish brown), toluene (flesh pink to lavender), and xylene (yellow to pink), and interference from other solvent vapours present was minimal when a benzene concentration of 50 p.p.m. was superimposed on concentrations of solvents such as butyl alcohol, butyl acetate, and ethyl acetate which gave slight yellow coloration under saturated conditions. The impregnated silica gel method lends itself to the technique introduced by Tiselius in 1943 and known as the " displacement " technique, which may be used for various analytical purposes.

It has been described by Övrum (1956) in the determination of atmospheric benzene. The principle is that of adsorption of the fluid mixture to be analysed on a column of silica gel, with subsequent displacement by a substance which is more strongly adsorbed than any of the components of the mixture. The adsorbed benzene is forced out of the gel by absolute alcohol and collected in a volumetric flask, then identified and measured by an ultra-violet spectrophotometer, using absolute alcohol as the spectroscopic solvent. Concentrations ranging from 0·003 to 1·28 mg. per litre were determined without difficulty by this method. Other physical methods of estimation of atmospheric concentrations include those of catalysed combustion, vapour pressure, absorption spectrophotometry, and chromatography.

Catalysed Combustion.—In catalysed combustion over a heated platinum wire, the temperature increase of the wire is measured electrically; the method is sensitive enough for many organic substances—hydrocarbons, alcohols, ethers, and esters (Strafford, 1949).

Vapour Pressure Method.—In the vapour pressure method, organic vapours are condensed by means of a freezing agent and then allowed to warm to room temperature and the pressure measured with a manometer (Couchman and Schulze, 1939; Silverman, Reece, and Drinker, 1939).

Absorption Spectrophotometry.—This method is ideally suited for automatic recording, and although the necessary instruments are costly and need considerable servicing, they have already been applied to substances such as carbon disulphide, aniline, trichloroethylene, and perchloroethylene, and will no doubt be more generally used in the future.

Gas Chromatography.—Gas chromatography is specially suitable for estimating the separate components of a solvent mixture. The size of sample required is very small, amounting to less than 5 ml. for a gas or less than 20 ml. for a liquid. The solvent is carried, by means of a carrier gas, which may be a stream of helium, argon, hydrogen, nitrogen, or carbon dioxide, flowing at a controlled rate, on to a stationary phase, which may be a solid such as alumina, silica, or charcoal, or a liquid supported on a highly porous inert material such as diatomaceous earth (Talvitie, 1958). Those components with the highest solubility in this stationary phase are held longest on the partition column, so that each component emerges separately in the carrier gas and is determined quantitatively by a detector. Various types of detector are available, depending upon which property of the carrier gas is to be measured—thermal conductivity, gas density, or flame temperature if the carrier gas is combustible. The newest detector, depending on measurement of the ionization of the current induced by Beta rays, can detect less than 1 p.p.m. of solvent. The peak area of each component as it appears on a strip chart recorder is a measure of its concentration and the analysis has an accuracy of 0·05%.

INDIVIDUAL SOLVENTS

The Aromatic Hydrocarbons

Among the aromatic hydrocarbons benzene is unique in its specific attack on haemopoietic tissue. The metabolic studies already described have shown that none of its homologues produces end-products with a special affinity for bone marrow, though one, p-tertiary butyl toluene, which will be described in detail later, is said to have produced a peripheral blood disturbance suggestive of a "benzene" effect. One of the main features of the more recent investigations of solvents of this group has been the search for substances which might replace this technically valuable but most toxic member.

That the serious effects of benzene have not yet by any means been completely prevented is emphasized by a recent report (Savilahti, 1956) of more than 100 cases of chronic poisoning in one shoe factory in Germany where the air concentrations were later estimated at 400 p.p.m. Suspicion of toxic exposure was only aroused when two of the workers were admitted to hospital suffering from aplastic anaemia. Blood examinations of 147 workers were then made, with the result that 47 showed leucopenia (under 3,000 white cells per c.mm. in 18 cases), 51 anaemia, and 91 thrombocytopenia. Savilahti, in common with other German investigators, regards thrombocytopenia as the most frequent finding in chronic benzene poisoning. Although he found no definite correlation between a low thrombocyte count and a tendency to haemorrhage, he observed that the best prognosis was in those cases where thrombocytopenia was the only abnormality of the blood picture.

In the search for substances to replace benzene many solvents with similar technical properties have been suggested; they include trichloroethylene, perchloroethylene, the solvent naphthas, cyclohexane, and the various homologues of benzene, xylene, toluene, ethyl benzene, and certain commercial alkyl benzenes. Some of these have technical and economic disadvantages, while others may possibly contain small amounts of benzene as an impurity. This last possibility applies to the best known homologues of benzene, xylene and toluene, and to the light and heavy solvent naphthas. The light naphthas may consist of 70% xylene, 5%

toluene, and 25% cumene, and the heavy variety of 35% xylene and 50% cumene (Albahary, 1955). According to Elkins and Pagnotto (1956), analysis of eight samples of solvent naphtha indicated benzene concentrations from 0·6 to about 7%. The investigations of Fabre *et al.* in 1952 led them to conclude, on the basis of animal experiments, that cyclohexane had no injurious effect on the blood and was therefore a suitable substitute for benzene. It was later announced by Tara (1953) that two men and a woman employed in processes involving the use of cyclohexane had shown peripheral blood changes similar to those of chronic benzene poisoning. Truhaut replied to these observations by stating that his examinations of samples of commercial cyclohexane had revealed the presence of benzene in amounts varying from 1 to 3·6 g. per 100 ml. and that in using cyclohexane as a substitute for benzene its freedom from benzene as an impurity must be rigorously controlled.

Among the less well-known homologues of benzene which have recently undergone investigation are certain alkyl derivatives, including iso-propyl benzene (cumene), n-propyl, n-butyl, methyl, trimethyl, tetra-methyl, amyl, ethyl, propyl, and methyl-propyl benzenes, styrene, α-methyl styrene, and vinyl toluene. These substances have been tested by Gerarde (1956) with a view to determining whether they possess the benzene-like specificity for haemopoietic injury, and some of them for their neurotoxicity relative to that of benzene (Furnas and Hine, 1958). These commercial alkyl benzenes, used extensively as solvents for fats, resins, and rubber, are petrol derivatives obtained by catalytic hydrogenation of petroleum products. In Gerarde's experiments they were administered to animals subcutaneously in olive oil, while control groups received benzene in olive oil or olive oil alone. The criteria of injury were the general condition, peripheral leucocyte count, haematocrit value, marrow nucleated cell count, estimation of marrow ribonucleic acid and deoxyribonucleic acid, and microscopic examination of tissues and organs. It was found that as a group the alkyl derivatives showed a much lower toxicity in all these respects than benzene itself, particularly with regard to the blood findings. Whereas the benzene-treated animals showed leucopenia and a decrease in the marrow nucleated count and nucleic acid, those given the same dosage of toluene, ethyl benzene, n-propyl benzene, and n-butyl benzene showed no abnormality of any of these haemopoietic features.

Similar results were obtained by Wolf, Rowe, McCollister, Hollingsworth, and Oyen (1956), who gave animals repeated inhalations over a period of six months. They found that ethyl benzene, iso-propyl benzene, styrene, α-methyl styrene, and vinyl toluene were all less toxic than benzene and that none possessed its specific dyshaemopoietic effect.

The lack of toxic effect of iso-propyl benzene on the blood of animals was confirmed by Fabre, Truhaut, Bernuchon, and Loisillier (1954), but their biological investigations revealed a slow elimination, and therefore a possible cumulative action of this solvent. Paper chromatography showed the presence of some not fully identified phenolic derivatives in the bone marrow, brain, spleen, and adrenals; these organs showed no significant lesions, but in 10% of the animals there was some tubular nephritis. This is a very interesting finding, in view of the fact that the metabolic products of most of the alkyl derivatives are alcohols and carboxylic acids, which are of a low order of toxicity, unlike the phenolic compounds of benzene metabolism.

The acute effects on the central nervous system of the aromatic hydrocarbon solvents are well known, and the opinion has long been held that xylene and toluene are in fact more potent narcotics than benzene.

An attempt to confirm this by studying their effects on nervous tissue, and whether other derivatives of the series have a similar neurotoxic effect has recently been carried out by Furnas and Hine (1958). Large sublethal doses of the materials tested, which included benzene, toluene, xylene, ethyl toluene, methyl styrene, cumene, p- and m-tertiary butyl toluene, were administered to rats by injection; the degree of injury was assessed by histological examination of nervous tissues, by electroencephalography, and by oxygen uptake studies on brain tissue slices. It was confirmed that benzene was the least toxic in this respect and toluene the next, while the toxicity of the substituted toluenes increased from p-methyl up to p-tertiary butyl, the last causing marked cerebral stimulation followed by profound depression. Histological changes in the central nervous system were not found, even with p-tertiary butyl toluene, contrary to the findings in an earlier investigation by Ungar, Hine, Kodama, and Anderson (1955), who used special nerve tissue stains by which they were able to demonstrate deposits of metachromatic material in the glial elements of the brain and spinal cord, destruction of neurons, and patchy demyelination.

Tertiary Butyl Toluene.—As a result of the investigations of Hine, Ungar, Anderson, Kodama, Critchlow, and Jacobsen in 1954, and Furnas and Hine in 1958, p-tertiary butyl toluene appears to be incriminated as both a neurotoxic poison, affecting primarily the white matter, and also to some extent

as a dyshaemopoietic agent with an effect resembling that of benzene though not so severe.

p-Tertiary butyl toluene (1-tert-butyl-4-methyl-benzene), $CH_3C(CH_3)_3$ is a liquid with a distinctive odour (B.P. 192·8°C., sp. gr. 0·8573). Saturated air at room temperature contains 850 p.p.m. It is used chiefly as a stable, moderately high-boiling solvent, of high purity, for the preparation of resins.

Toxic Effects on Animals.—The results of intragastric administration as well as of inhalation of high concentrations show that the acute toxic effect of p-tertiary butyl toluene is greater than that of benzene, toluene, and cumene. The L.D. 50 for benzene is 10,000 p.p.m., for toluene 5,000 p.p.m., and for cumene 2,000 p.p.m.; that of p-tertiary butyl toluene is approximately 180 p.p.m.

Single exposures to inhalation of concentrations from 60 to 1,500 p.p.m. for periods varying from one to eight hours showed that the higher concentrations affected chiefly the central nervous and respiratory systems, causing paralysis of both spastic and flaccid types, and in some animals convulsions and epileptiform seizures. The lowest concentration at which muscular weakness appeared was 90 p.p.m. after an exposure of about six hours. Respiratory disturbances appeared at 60 p.p.m. and extreme immediate dyspnoea at 1,500 p.p.m. Short repeated exposures to saturated vapour concentrations (about 850 p.p.m.) also produced impairment of muscle tone and at relatively low concentrations degenerative lesions in the brain and spinal cord were observed at necropsy.

Animals repeatedly exposed showed a decrease in erythrocytes and leucocytes in the peripheral blood.

Toxic Effects on Human Beings.—The effects of p-tertiary butyl toluene on some workers employed in a pilot-scale production of this substance, as well as some sensory studies on volunteers, have been described by Hine *et al.* (1954). The concentrations to which the workmen were exposed were only about 10 p.p.m. during normal operations, but at times, owing to spillage or improper operation of the exhaust system, they might rise to 136 p.p.m. while 350 p.p.m. were found at the opening of the centrifuge when it was being hand scraped. Some of the men showed a low-grade transient intoxication, with symptoms of disturbance of the cardiovascular and central nervous systems—decreased blood pressure, increased pulse rate, tremor, and anxiety. There were also decreased levels of haemoglobin and red cells, leucopenia, and abnormal differential counts. Sensory response studies showed that exposure for five minutes to concentrations of 5 to 160 p.p.m. caused moderate eye irritation at 80 p.p.m. and giddiness and decreased respiratory effort in one subject at 160 p.p.m. Olfactory recognition was immediate at 5 p.p.m. The maximum allowable concentration recommended by the American Conference of Governmental Industrial Hygienists is 10 p.p.m.

The Chlorinated Hydrocarbons

The narcotic action of the halogenated hydrocarbons is well recognized, while some of them can also injure the liver or kidneys. The most toxic of the whole group, tetrachloroethane, partly as a result of experience in the aviation industry during the first world war, now has a somewhat restricted industrial application.

Controversy on the toxicity of the various members of the group has mainly related to their capacity for producing liver damage, especially with chronic exposure, and in the case of trichloroethylene whether it can be regarded as a liver poison at all. Many French investigators are convinced that trichloroethylene is not so innocuous in this respect as has hitherto been believed; nor do some of them agree that perchloroethylene, regarded by most authorities as one of the least toxic chlorinated hydrocarbons, should be considered a harmless substitute for trichloroethylene.

Trichloroethylene.—Trichloroethylene is a colourless liquid with a not unpleasant odour [B.P., (technical variety, 86·2 to 87·2°C., stabilized, 86 to 88°C., sp. gr. 1·469 to 1·475]. It vaporizes easily at ordinary temperatures, and is not inflammable, but under the influence of strong light or catalysts, such as aluminium dust, may decompose, with formation of HCl, and in contact with a naked flame may give rise to phosgene. Its industrial uses cover a wide field, particularly as a degreasing and cleansing agent.

Toxicity.—The question of trichloroethylene intoxication has received much investigation in recent years and many authorities consider that it should be placed higher in the list of toxic chlorinated hydrocarbons than its threshold limit value of 200 p.p.m. would indicate.

Effects on the Nervous System.—The acute narcotic effects of trichloroethylene have always been recognized; its powerful anaesthetic properties have in fact been widely used in surgical practice. It is on the question of its chronic effects that dispute has arisen. The numerous symptoms attributed by Stüber (1931) to chronic intoxication have been to some extent discounted by other observers, partly on the hypothesis that the trichloroethylene used in her investigations contained impurities which may have been responsible for some of the disturbances

listed. An investigation in 1955 by Grandjean *et al.*, however, revealed a high incidence of neurological disturbances, including nystagmus, modification of vision and of sensory reflexes, slow tremors, and ataxia in 14 of 50 workers examined; vegetative disorders (excessive perspiration, fine tremors, functional gastro-intestinal, and circulatory disorders) in 18, and psychical disturbances in eight. These symptoms were present when the air concentrations varied between 20 and 80 p.p.m.

Effect on the Liver.—There has always been some debate on the question whether trichloroethylene is a liver poison, and the majority opinion has been that it differs from the other chlorinated hydrocarbons in this respect. In the few cases where trilene anaesthesia has been followed by liver damage (Herdman, 1945; Dodds, 1945) it has been suggested that the cause was not trilene itself but decomposition products formed in the closed circuit machine with a soda lime absorber. In a fatal case reported in the *Lancet* (1944), in a child of 2 years, however, in spite of the fact that the anaesthetic was given by an open mask, the liver showed central necrosis similar to that seen in delayed chloroform poisoning. Evidence of liver disease after ingestion of trichloroethylene has recently (1956) been reported by Lamotte, Caroit, and Nathan and after severe industrial exposure by Carrié, Perrault, and Bourdin (1941), and Dérobert, Hadengue, Martin, and Prachet (1952), while Germain and Marty (1947) described a fatal case of hepato-nephritis in a man who had used trichloroethylene as an addition to a paint which he had used for three and a half hours in a small room. The liver showed areas of necrosis and fatty degeneration and the kidneys severe tubular nephritis. Other French authorities have observed hepatitis in experimental animals (Fiessinger and Loeper, 1941), as also has Seifter (1944), while liver involvement has been noted in cases of acute trichloroethylene intoxication with oedema of the lung (Vallée and Leclerq, 1935) but the evidence of liver damage from chronic industrial exposure is not convincing.

The best record of an industrial case is that of Carrié, *et al.* (1941) in an employee of a shoe factory who developed severe jaundice and died. The liver was small, intensely bile-stained, with central necrosis and basophilic cell infiltration.

The case reported by Joron, Cameron, and Halpenny in 1955 is exceptional in attributing a fatal massive necrosis of the liver to a trichloroethylene exposure of not more than two and a half hours every two or three weeks for 18 months. The man, a chemist in a plant where trichloroethylene was used as a solvent, stated that he had always worn a mask except on one occasion, the day preceding that on which nausea and extreme fatigue became superimposed on general fatigue from which he had suffered for some months. He became jaundiced, developed ascites, and died in coma a month later. The liver showed acute necrosis with no productive fibrosis. Analysis of the air in the room where he had supervised the preparation of a solution used for processing paper, involving the mixing of trichloroethylene, paraffin, and resin, showed concentrations up to 297 p.p.m. during the mixing when doors and windows were closed and up to 200 p.p.m. when they were open.

Effects on the Blood.—Various changes in the blood picture of persons exposed to trichloroethylene have been recorded from time to time, but the consensus of opinion (with which the author, from personal observations, agrees) is that these are not specific, and do not represent a true dyshaemopoietic effect. In one of the most comprehensive recent surveys of chlorinated hydrocarbon solvents (Vallaud, Raymond, and Salmon, 1956), it is recorded that the blood picture of a number of employees exposed to tri- and perchloroethylene was remarkably constant, the only variation being a slight initial polycythaemia returning to normal within a few months. This observation has been confirmed still more recently by Guyotjeannin, Fournier, and Guyotjeannin (1958), following an investigation of 75 workers using pure trichloroethylene as a degreasing agent. These men showed trichloracetoaciduria and typical symptoms of chronic trichloroethylene intoxication (fatigue, headache, nausea, vertigo, dizziness). Only very slight, infrequent and insignificant variations of the blood picture were present in a few cases. These observers conclude that trichloroethylene is not toxic to the haemopoietic system.

Sudden Deaths in Trichloroethylene Workers.—" Mysterious sudden deaths " have been reported in trichloroethylene workers, usually during periods when they were not exposed and often following exertion: at necropsy no gross anatomical changes were found which could be held responsible, and several hypotheses have been advanced to account for the cause of death. Among these are primary cardiac failure, ventricular fibrillation, and anoxia due to tachypnoea and impaired alveolar ventilation. Cardiac arrhythmia causing syncope is not uncommon during inhalation of trilene for anaesthetic purposes. Such cases have been recorder by Geiger (1943) and by Waters, Orth, and Gillespie (1943), while Bernstine (1954) observed ventricular tachycardia and fibrillation in a case under trilene analgesia.

In four industrial cases where death occurred a

short time after cessation of exposure, Kleinfeld and Tabershaw (1954) attributed the cause to cardiac arrhythmia, as also did Bell (1951) in a similar case occurring in a dry cleaning establishment. In all these cases it was found that there had been previous complaints of occasional nausea and giddiness, but actual collapse and death were sudden, either while travelling home, or, in one case, a night watchman who cleaned metal parts with trichloroethylene during his shift, unobserved during the night.

Trichloracetoaciduria.—Since Barrett and Johnston in 1939 demonstated trichloracetic acid in the urine of dogs narcotized by trichloroethylene, the quantitative aspect of the relation between trichoroethylene exposure and the amount of trichloracetic acid excreted in the urine has provided useful information as to the efficacy of the plant and ventilation in workshops where trichloroethylene is used, but the wide variations in individual excretion do not permit its being used alone without air analyses of the actual degree of exposure. Powell (1945), and Paykoc and Powell (1945) followed up the animal experiments by identifying trichloracetic acid in the urine of human beings anaesthetized by trilene, and showed that its elimination was slow; this observation has since been confirmed by other observers, including Grandjean *et al.* (1955), who found considerable amounts of trichloracetic acid in the urine up to 10 days after exposure.

From these observations attempts have been made to relate the amount of trichloracetic acid in the urine to the level at which exposure to trichloroethylene can be injurious. The ratio between the urinary trichloracetic acid excretion and the exposure to trichloroethylene was found by Grandjean to vary somewhat with age, the younger workers having an average ratio of 6:1, the older men 2:1, the average for men occupied for the whole day on a trichloroethylene plant being 3:1. It was found that about 13% of the trichloroethylene inhaled during a work period of eight hours was eliminated as trichloracetic acid. (An investigation of workers in dry cleaning establishments by Bardoděj and Krivucová in 1955 gave a figure of 5 to 8%.)

Correlation between the appearance of symptoms and the urinary concentration of trichloracetic acid has been postulated by some observers but not confirmed by others. Ahlmark and Forssman (1951) found such a correlation and suggested that the limit of tolerance of excretion of trichloracetic acid should be fixed at 20 mg. per litre, corresponding to an exposure to trichloroethylene concentrations of 5 to 10 p.p.m. Grandjean *et al.* found symptoms appearing with an average air concentration of 40 p.p.m. Hickish, Smith, and Bedford (1956), investigating the atmospheric exposure, urinary trichloracetic acid, and clinical findings in three employees on a degreasing plant found that at various positions the concentrations of trichloroethylene vapour varied from 62 to 637 p.p.m., the 24-hour urinary excretion of trichloracetic acid from 175 to 258 mg. per litre, and that at these levels vague symptoms of fatigue, headache, and occasional vertigo, with no detectable clinical organic disturbance, were present. Correlation of symptoms with trichloracetic acid excretion has not been confirmed by Frant and Westendorp (1950) or by Bardodéj Vyskočil (1956), but the use of the amount of trichloracetic acid in the urine as a criterion of the actual amount of exposure seems to have found favour in many quarters. A simple field test for this purpose has been described by Engel (1956). His test for trichloracetic acid was based on the Fujiwara reaction as described by Frant and Westendorp in 1950, and modified by Waldman and Krause in 1952, using a spectrophotometer. In Engel's method a Lombard colorimeter with a series of standard coloured discs is used and the results are read in milligrams per litre in nine stages from 12·5 to 200 mg. per litre. The present maximum allowable concentration of trichloroethylene suggested by the American Conference of Governmental Industrial Hygienists in 1958 is 200 p.p.m., a value far above that of 5 to 10 p.p.m. (corresponding to a trichloracetic acid excretion of 20 mg. per litre) suggested by Ahlmark and Forssman, or the 40 p.p.m. (corresponding to a trichloracetic acid excretion of 96 mg. per litre) by Grandjean *et al.* The only countries where such low levels of air concentrations of trichloroethylene are actually insisted upon are Russia and Czechoslovakia, where the limit is 9 p.p.m.

Perchloroethylene. — Perchloroethylene (tetrachloroethylene, ethylene tetrachloride) has until recently been regarded as one of the least toxic of the halogenated hydrocarbons, especially with respect to its action on the liver, and has been proposed as a substitute for trichloroethylene, but some recent investigations seem to indicate that this view of its relative non-toxicity may be unfounded.

Perchloroethylene is a colourless, non-inflammable liquid with a slight ether-like odour (B.P. 121°C., sp. gr. 1·610). It is used chiefly as a degreasing agent but also as a dry cleaner.

Toxicity.—As a narcotic agent perchloroethylene is slightly more powerful than trichloroethylene (Lazarew, 1929).

In animals both single and long-continued exposures to high concentrations (up to 2,300 p.p.m.)

have produced only slight liver damage (Lamson, Robbins, and Ward, 1929; Carpenter, 1937). In human beings few cases of acute injury which could be definitely attributed to perchloroethylene have been recorded. A case of fatal hepato-nephritis with pulmonary oedema was reported by Vallaud *et al.* in 1956, but the conditions were not precisely described, and another, by Beyer and Gerbis, in 1931, in which the cause of death was stated to be liver degeneration, was of doubtful origin as perchloroethylene was not the only constituent of the dry-cleaning solvent used. A fatal case recorded by Lob, in 1957, in conjunction with his description of other slighter cases of intoxication in the same factory, is more definitely attributable to perchloroethylene. The fatal case was of a builder employed in installing vacuum exhaust for a perchloroethylene plant; after being seized with nausea and faintness he died suddenly. The cause of death was pulmonary oedema. Two other workers on the plant showed severe neurological disturbance similar to that reported from chronic trichloroethylene intoxication, including tremors, disturbance of equilibrium, difficulty in walking, and abnormal sensory reactions. Seven others, after being employed from three weeks to eight months, complained of less severe symptoms—weakness, dizziness, headache, nausea, vomiting, anorexia, and irritability—which disappeared on stopping work. The air concentrations of perchloroethylene were found to be about 75 p.p.m. A similar syndrome was noted by Coler and Rossmiller, in 1953, in workers engaged in degreasing metals twice a week, where the air concentrations were 230 to 380 p.p.m. These workers showed in addition slight changes in hepatic function.

It is concluded that perchloroethylene, if used as a substitute for trichloroethylene, which has the same threshold limit value (200 p.p.m.), must be used with the same precautions.

Carbon Tetrachloride (Tetrachloromethane) CCl_4.—Carbon tetrachloride is a colourless, non-inflammable liquid with an odour rather like that of chloroform (B.P. 75·7 to 76·7°C., sp. gr. 1·600 to 1·608). Carbon tetrachloride has found a wide application during recent years in the manufacture of refrigerants and as an insecticide dispersant; its use as a dry-cleaning agent has decreased considerably, but it is still used extensively as a fire extinguisher.

Toxicity.—The acute effects of carbon tetrachloride poisoning—narcosis, liver and kidney injury—are so well known and the means of preventing them in industrial processes so widely recognized that they have become much less frequent of late years. It is evidently realized, from the fact that the threshold limit value has been reduced from 100 p.p.m. to 25 p.p.m. that the quantities likely to produce toxic effects on the liver and kidneys are not so great as was formerly believed. The account (Occupational Health News, 1956) of a non-industrial fatality, when only about 1 pint of CCl_4 had been used to clean a carpet in an apartment, whose owner died 10 days later from toxic hepatitis and renal insufficiency, is a reminder that susceptible persons may respond adversely to concentrations considerably lower than those once regarded as the safety limit for acute poisoning; as late as 1931 the Retail Credit Company of Atlanta suggested 1,600 p.p.m. as a safe level for short-term exposure. The actual concentration in the room in which the above case occurred was 63·5 p.p.m. Whatever the route of administration, most fatal cases develop symptoms after a delay of one to three days and survive a week or more. The damage to internal organs is usually most marked in the liver; in other cases the kidneys are more severely affected, and in all there is some lung involvement.

The actual mechanism of the liver injury, and the processes of regeneration have been described by several observers. Its connexion with enzymatic activity has been investigated by Christie and Judah (1954) and, with the help of paper chromatography, by Wahi, Tandon, and Bharadwaj (1955). It appears that the primary assault by carbon tetrachloride on the mitochondria of the liver cell causes enzymatic disorganization and initiates changes in protein metabolism, with conversion of cellular proteins to amino-acids. If these changes are so marked that the cell cannot survive, necrosis follows and autolysis of the necrosed cells causes a further rise in free amino-acid concentration. In other cells, particularly those at the periphery, the alterations are less marked, and, if minimal, recovery soon follows. This process of recovery and the capacity of the liver for regeneration when exposure has ceased was the basis of the view expressed by Stewart and Witts in 1944 that the gastro-intestinal symptoms in many persons exposed to small repeated doses of carbon tetrachloride were not indicative of permanent liver injury. They pointed out that if each dose is too small to produce an initial tissue lesion, repeated exposure, however often repeated, will not cause hepatic damage, and that in animals at any rate, even when the liver damage has progressed perceptibly, the process may be reversible if exposure ceases. To bring about permanent damage there must be exposure sufficient to produce an immediate toxic effect, and the dose must be repeated at short intervals. Nevertheless, the dose required to produce the initial lesion is not large.

The importance of renal injury has also been

emphasized in recent years, many observers considering it to be more frequently associated with inhalation of carbon tetrachloride than liver damage, which is predominant in cases of poisoning by ingestion (Simon, 1939). Umiker and Pearce (1953) believe that whereas the usual cause of death during the first week is hepatic failure, renal insufficiency with uraemia is the essential feature of deaths occurring after this time. The oliguria which develops within two to eight days of acute exposure is explained (Sirota, 1949) by back diffusion of the glomerular filtrate across the damaged tubule walls; in prolonged oliguria or anuria there is a marked diminution in renal blood flow, the resulting anoxia, together with the initial toxic effect, causing maximum depression of tubular function (Kirkpatrick and Sutherland, 1956). The presence of protein and blood in the urine suggests abnormal glomerular permeability. Complete recovery in favourable cases is associated with re-establishment of the tubular barrier and active epithelial regeneration of the affected nephrons; in such cases there appears to be no residual renal lesion.

Trichloroethane (Methyl Chloroform).—Trichloroethane, which has not hitherto been widely used in industry, is now being strongly recommended as a substitute for other better known solvents such as trichloroethylene, tetrachloroethylene, and especially carbon tetrachloride, partly because of its technical advantages, partly because of its alleged relative non-toxicity. This latter claim is based largely on the results of animal tests, and has been accepted in several countries. In Pennsylvania, following two cases of carbon tetrachloride poisoning, one of which proved fatal, a large electrical firm has recommended the use of a number of substitutes, containing methyl chloroform in varying proportions, for degreasing and cleansing purposes. One of these (" penetone 602 ") is a mixture of 25 to 30% of methyl chloroform with mineral spirit; another (" dynasol ") consists of 94% methyl chloroform and 6% inhibitor.

There are two isomers of trichloroethane, the α or 1.1.1-trichloroethane and the β or 1.1.2-compound. Both are liquids, the α isomer boiling at 74·1°C. and the β isomer at 113·5°C. Trichloroethane is not inflammable and may be used without decomposition in the absence of air and water at temperatures up to 110°C. (McGovern, 1943). In contact with water it hydrolyses appreciably at its boiling point. The National Safety Council (1957) advises that it should not be used as a fire extinguisher since irritating and toxic gases may be produced in contact with flame, though less phosgene is produced than with carbon tetrachloride.

Trichloroethane is a solvent for oils, waxes, tars, many resins, alkaloids, and rubber, and is specially suitable for cleaning and degreasing, in which operations it shows a great similarity to CCl_4. Like CCl_4 it is miscible with alcohol, ether, acetone, and benzene; it also mixes with CCl_4. The technical grade will react violently with unoxidized aluminium and other metals, but this property has been eliminated from the stabilized forms.

Toxicity.—There is some disagreement about the relative toxicity of the two isomers. Lehmann and Flury (1943) stated that the α isomer was four times as toxic as the β isomer, but this has been denied by other observers (Adams, Spencer, Rowe, and Irish, 1950) and by Dr. Hecht, toxicologist of the Farbenfabriken Bayer (personal communication from Dr. Soehring of the Pharmacological Institute, Hamburg). Dr. Hecht states categorically that " the β isomer is certainly more toxic than the α isomer; the contrary opinion of Flury-Lehmann is wrong ". According to Lehmann both derivatives cause, in animals, irritation of the nervous system, some fatty deposition in the liver and kidneys, and oedema and haemorrhage of the lungs. Adams *et al.* (1950), however, also on the basis of animal experiments, state that trichloroethane is much less toxic than tri- or perchloroethylene, and about equal in toxicity to methylene chloride, which in its turn is considered about one tenth as toxic as carbon tetrachloride. The National Safety Council (1957), while stating that " there is no known case of human injury ", affirms that " the symptoms of poisoning in order of increasing severity are impaired coordination, dizziness, sleepiness, mental dullness, and unconsciousness ". Dermatitis and eye irritation may be produced by contact; the odour at 500 p.p.m. is perceptible but not disagreeable to most persons, and 1,000 p.p.m. can be tolerated occasionally for periods up to 30 minutes. The threshold limit value of trichlorethane is given as 500 p.p.m. as compared with 25 p.p.m. for carbon tetrachloride, and according to the Hygienic Guides Committee, general ventilation is sufficient for brief exposures or those resulting from very small quantities of the solvent: with prolonged exposure to high temperature operations exhaust ventilation is required.

The Ketones

The ketones have generally been regarded as having no significant toxic effect apart from their narcotic properties when inhaled in high concentrations, and with the exception of isophorone, their place in the list of threshold limit values seems to confirm this view. Most of them range from 100 p.p.m. (methyl butyl " hexanone "), to 1,000 p.p.m. (acetone), but the level suggested for iso-

phorone is 25 p.p.m. It appears, however, that when used in combination, the synergistic effect may produce higher toxicity than that of one ketone used alone. Smith and Mayers (1944) have reported that acetone and methyl ethyl ketone in combination may have an effect on the central nervous system which outweighs that of either; such a combination has caused acute intoxication in two cases in the United States during the manufacture of waterproof material (*Industrial Accident Prevention Bulletin*, 1946 vol. 14, (132), p.2).

Isophorone.—Isophorone has become a widely used solvent in the lacquer and plastics industry since its introduction in 1940, and is recognized as one of the most powerful solvents of the ketone series for nitrocellulose and polyvinyl resins.

Isophorone (isoacetophorone, 3, 5, 5-trimethyl-2-cyclohexene-1-one) is a liquid with a peppermint-like odour (B.P. 215·2°C., sp. gr. 0·9229).

Toxicity.—While isophorone has caused no recorded injury in human beings from its industrial use apart from irritation of mucous membranes at a level of 25 p.p.m. (Silverman, Schulte, and First, 1946) it appears to produce in animals a cumulative injury to the kidneys. Repeated inhalation of concentrations above 100 p.p.m. caused the death of 12 to 45% of the animals, and though only those exposed to 500 p.p.m. showed albuminuria, the kidneys of others showed congestion, and the lungs were also affected, with desquamation of bronchial epithelium, microscopic haemorrhage, and sometimes pneumonia. A colorimetric method for the determination of small amounts of isophorone in air, based on its reaction with phosphomolybdic acid, has recently been devised by Kacy and Cope (1955).

Di-isobutyl Ketone.—The only other ketone which has been recently investigated in detail is di-isobutyl ketone.

Di-isobutyl ketone (2-6-dimethyl heptanone-4) has a boiling point of 168·1°C. and specific gravity of 0.8089. It is used chiefly as a solvent for nitrocellulose, crepe rubber, synthetic coatings, and certain resins.

Toxicity.—Up to 1953 the results of experiments on animals, though providing on the whole evidence of its relative lack of toxicity, were somewhat conflicting. An investigation in that year, including observations on human subjects, confirmed that di-isobutyl ketone, apart from slight symptoms of discomfort attributable to the narcotic properties common to all ketones, causes no significant systemic injury.

Animal Experiments.—In 1949, Smyth, Carpenter, and Weil reported that while the single oral toxicity to rats was low, inhalation of 2,000 p.p.m. for eight hours was fatal to five out of six. In the same year, however, McOmie and Anderson found that single and repeated inhalation of saturated vapours indicated a somewhat lower level of toxicity. This latter conclusion was confirmed by an extensive investigation by Carpenter, Pozzani, and Weil in 1953, their animal experiments being supplemented by observations on two human subjects. The animals were exposed for seven hours daily for 30 days to concentrations ranging from 125 to 1,650 p.p.m. No significant damage was observed at 125 p.p.m. and major damage and mortality only at 1,650 p.p.m.; in between these levels there was some increase in weight of the liver and kidneys.

Tests on Human Subjects.—Human subjects tested by Silverman *et al.* in 1946 for their sensory response estimated that 25 p.p.m. was the highest concentration tolerable for an eight-hour exposure. Those examined by Carpenter *et al.* inhaled 50 and 100 p.p.m. of the vapour of di-isobutyl ketone for three hours and showed only slight irritation of the eyes, nose, and throat. There was no significant change in pulse rate or blood pressure, and tests for urinary sugar and albumin were negative. Simple coordination tests also showed no disturbance and the only symptoms of discomfort were slight headache and giddiness on returning to fresh air. They agreed that a workroom atmosphere of 50 p.p.m. would be satisfactory, and 100 p.p.m. unsatisfactory.

The Glycols and Glycol Ethers

Ethylene glycol itself and the more toxic of its derivatives appear to have a special predilection for the kidneys, but some of the ether derivatives, notably methyl cellosolve, have been reported to affect the central nervous system, and butyl cellosolve has recently been incriminated as a haemolytic agent.

Ethylene Glycol.—Ethylene glycol, owing to its low volatility, has usually proved toxic only by ingestion, and in factories in the United Kingdom there has been little or no evidence of a toxic effect from its fumes, but some unusual manifestations following chronic exposure have been reported from Italy.

Ethylene glycol (glycol alcohol) is a clear, syrupy hygroscopic liquid with a sweetish taste (B.P. 197·85°C., sp. gr. 1·1136). It is used to some extent as a solvent for food and toilet preparations, but chiefly as an anti-freeze agent for automobile radiators.

Toxicity.—From 1930 onwards, many cases of severe poisoning, some of them fatal, have been recorded following ingestion, either accidental or

purposeful, and in all the pathological changes have been consistently and predominantly renal. A well-documented non-fatal case, in which biopsy of the kidney revealed the characteristic lesions, was that described by Ross in 1956 of a man who had drunk a quarter to half a pint of anti-freeze and developed not only anuria but also meningo-encephalitis. The kidney biopsy showed marked destruction of epithelial cells and deposition of calcium oxalate in the tubules. The agent responsible for this toxic effect on the kidneys is believed to be the chief metabolite of ethylene glycol, oxalic acid. The amount of this product recoverable from the urine is 3 to 10%; therefore the amount derived from 100 ml. of ethylene glycol is 3 to 10 g., and according to Jeghers and Murphy (1945) a dose of 2 g. of oxalic acid may be fatal.

Propylene Glycol.—This is possibly the only derivative of glycol which is believed to have no direct toxic action on the kidneys, and this has been explained by the fact that it does not form oxalic acid as a metabolite (Berman, Schreiner, and Feys, 1957).

Chronic industrial poisoning from ethylene glycol is, as already mentioned, rare, but a few cases reported in England had some albumin and red corpuscles in the urine (Browning, 1952). An unusual effect of chronic exposure was described by Troisi (1950) in a group of women engaged in the manufacture of electrolytic condensers. One phase of the work involved the spreading by hand of a mixture of 40% ethylene glycol, 55% boric acid, and 5% ammonia. In this operation, because of the necessity to keep the receptacles at a temperature of 105°C., exposure to the vapour of ethylene glycol was inevitable. The symptoms were those of periodic attacks of loss of consciousness, lasting only five to 10 minutes and followed by no apparent discomfort. Ten of the 38 women employed showed well-defined nystagmus, which was interpreted as being of supra-nuclear origin without involvement of the vestibular apparatus. Both the nystagmus and also the attacks of unconsciousness disappeared when the process was operated in a closed plant.

Methyl Cellosolve.—While methyl cellosolve has been known to cause toxic changes in the kidneys of animals by ingestion, its chief toxic effect from industrial exposure has been related to the central nervous system; it can also cause anaemia of the macrocytic variety.

Methyl cellosolve (ethylene glycol monomethyl ether, 2-methoxyethanol) is a colourless, stable liquid with a faint, not unpleasant odour (B.P. 124·5°C., sp. gr. 0·967). It is used in the lacquer industry, and as a solvent in the manufacture of " fused collars ", where the lining of cellulose acetate is soaked in a solvent containing about 33% of this substance; when heat and pressure are applied the collar becomes permanently stiffened.

Toxicity.—The principal industrial effect of methyl cellosolve recorded has been " toxic encephalopathy ", with symptoms of lassitude, sleepiness, giddiness, severe frontal headache, and a change of personality from intelligence and quickness to stupidity and lethargy (Parsons and Parsons, 1938). Moderate ataxia was present in the two cases reported by these authors and also in one recorded by Donley (1936), while Greenburg, Mayers, Goldwater, Burke, and Moskowitz (1938) noted abnormal reflexes, tremor of the hands, and mental retardation. All these workers were employed in the fused collar process, and some of them showed a macrocytic anaemia.

Butyl Cellosolve.—Butyl cellosolve (ethylene glycol mono-n-butyl ether) has been indicted on the basis of animal experiments as a haemolytic agent, though it is not unique among the glycol derivatives in this respect; methyl cellosolve acetate, cellosolve, and butyl ethyl cellosolve appear to have the same propensity for causing erythrocyte fragility, but none of them appears to exert this effect strongly in human beings.

Butyl cellosolve is a colourless, mobile liquid with a slightly rancid odour (B.P. 170 to 176°C., sp. gr. 0·9188). It is used as a solvent for cellulose nitrate, resins, oils, and fats, and to some extent as a constituent of paints and lacquers.

Toxicity.—In addition to its action as a central nervous depressant and a kidney toxin, in which respects butyl cellosolve is considered to have a high toxicity relative to other members of this group, it causes marked haemolysis in rodents, but there is a variation in toxicity according to the species of animal and a still more marked difference between animals and human beings.

In rodents, the haemolytic effect is very evident with massive inhalation (Carpenter, Pozzani, Weil, Nair, Keck, and Smyth, 1956), the haemoglobin level being halved after inhalation for seven hours, and the number of red corpuscles being reduced even further. Osmotic fragility tests show a repeated pattern of increased fragility during exposure followed by a decrease to normal values after an overnight rest. This suggests that the older and weaker cells are being destroyed and promptly replaced. The haemolytic effect is not nearly so marked in dogs (Werner, Mitchell, Miller, and von Oettingen, 1943; Werner, Nawrocki, Mitchell, Miller, and von Oettingen, 1943) and is absent in human beings exposed to 200 p.p.m. for eight hours

whereas rats develop haemoglobinuria with 62 p.p.m. for four hours.

Metabolic studies carried out with the help of chromatography show that in animals and human beings most of the butyl cellosolve is excreted in the urine in the form of butoxyacetic acid. Human beings inhaling 195 p.p.m. for two four-hour periods with a half-hour interval excreted 175 to 300 mg. per 24-hour sample; with exposure to 100 p.p.m. for eight hours the 24-hour excretion was 100 to 200 mg. with individual variations (Carpenter *et al.*, 1956). They believe that butoxyacetic acid is more directly responsible for the haemolytic effect than butyl cellosolve itself, and that the chief reasons for the rarity of industrial injury from this solvent are its low volatility, the slow effect on the erythrocytes of the low concentrations thus available, and the fact that this is one of the solvents to which human beings are more resistant than animals.

The present recommended threshold limit value of 240 p.p.m. appears unlikely to cause human injury, but in view of the possibility that constant and rapid replacement of haemolysed red cells might eventually prove a strain on the erythropoietic system and cause some degree of haemolytic anaemia, 100 p.p.m. might be a more appropriate level.

The Propylene Glycol Methyl Ethers

The powerful solvent capacity for nitrocellulose and synthetic resins of these members of the glycol group, and the fact that they combine the chemical properties of alcohols, ethers, and hydrocarbons has brought them into industrial prominence during recent years.

	B.P. (°C.)	Sp. Gr.
Propylene glycol methyl ether	120	0·919
Di- " " " "	190	0·951
Tri- " " " "	243	0·967

They are all miscible with water and with acetone, benzene, ether, carbon tetrachloride, methanol, and a large number of other organic solvents.

Toxicity.—The principal toxic effect of all three compounds is narcosis, the mono-compound being most active in this respect. They appear to be comparable in acute and chronic toxicity by inhalation to methyl chloroform 1.1.1. trichloroethane) and in general systemic effect to other solvents, such as trichloroethylene and perchloroethylene, which are powerful narcotics but cause relatively little organic injury. They are to some extent skin irritants and can be absorbed by the intact skin. In animals, single 24-hour applications of 10 ml. per kg. of the mono- and 15 ml. per kg. of the di-compound caused some deaths. Repeated exposure over a period of six months to practically saturated atmospheres was followed by only slight general ill-effects but some narcosis and minor injuries to the lungs and liver (Rowe, McCollister, Spencer, Oyen, Hollingsworth, and Drill, 1954).

In human beings no injury has been recorded from the industrial use of these solvents, and skin sensitization tests with di-propylene glycol methyl ether showed no evidence of irritation or sensitization in 250 unselected subjects. It appears that there is little likelihood of toxic amounts of these compounds being absorbed by the skin or by inhalation. In the latter case, concentrations dangerous to life would be so objectionable that they would not be breathed voluntarily, and the highest concentration of the di-compound available at ordinary room conditions is 300 to 400 p.p.m., which was tolerated by animals with very little ill-effect and is quite disagreeable to human beings.

The effects of the tri-compound have not been evaluated, but Rowe *et al.* state that a saturated atmosphere at room conditions (about 50 p.p.m.) could probably be tolerated without ill-effects. Dipropylene glycol methyl ether is probably the safest of the three for uses involving prolonged or repeated contact with the skin.

Tetrahydrofuran

Tetrahydrofuran (diethylene oxide), a colourless liquid with an etheric odour (B.P. 65 to 66°C. sp. gr. 0·88), is one of the newer solvents which has been found to have excellent solvent properties for lacquers and resins, and so far, in spite of its chemical similarity to dioxane, there are no reports of neural damage from its industrial use, though there is some evidence of kidney injury in animals. A recent investigation by McCormick (1957) indicates that tetrahydrofuran is primarily a narcotic, no more potent than methyl ethyl ketone, and that it is safe to use in concentrations of 100 to 200 p.p.m. The skin irritation noted by Lehmann and Flury (1943) is believed (Hofmann and Oettel, 1954) to be due to decomposition products of the technical grade, such as peroxide, rather than to tetrahydrofuran itself.

Amines and Coal Tar Bases

The principal compounds of this group used as solvents are the ethanolamines, cyclohexylamine, and ethylene diamine. The ethanolamines, the tri-compound of which is industrially of the most importance, are relatively non-toxic, even as skin irritants and have no significant systemic toxicity. Cyclohexylamine and ethylene diamine, however, have both been recently incriminated as sensitizers

as well as direct skin irritants, and cyclohexylamine has been reported to cause some disturbance of health.

Cyclohexylamine (Hexahydroaniline, Aminocyclohexane).—Cyclohexylamine is a colourless, strongly basic liquid with a marked fishy odour (B.P. 134·5°C., sp. gr. 0·8647). It is used chiefly as a solvent for dyestuffs, as a dye intermediate, and as a vulcanizer in the rubber industry.

Toxic Effects.—Cyclohexylamine is a strong skin irritant and a moderately strong sensitizing agent (Mallette and von Haam, 1952). It is lethal to animals by injection or by inhalation of high (1,200 p.p.m.) concentrations (Watrous and Schulz, 1950), probably by its toxic action on the motor centres of the spinal cord and medulla (Carswell and Morrill, 1937). Systemic toxic effects of a mild and transitory character from industrial exposure have been recorded in three cases by Watrous and Schultz, in the form of drowsiness, nausea, and dilatation of the pupils, with vomiting in one case. Measurements of air concentrations showed that no symptoms arose at levels of 4 to 10 p.p.m. No threshold limits have yet been established for cyclohexylamine.

Ethylene Diamine (1,2, Diaminoethane).—Ethylene diamine is a hygroscopic liquid with an ammoniacal odour (B.P. 117·2°C., sp. gr. 0·8895). Although ethylene diamine finds its chief application in the chemical industry as an intermediate in the synthesis of organic compounds, it is also used to some extent as a solvent for water-insoluble acids, resins, and gums.

Toxicity.—Ethylene diamine is an irritant to skin and mucous membranes and can cause burns. Its chief disadvantage from the point of view of industrial exposure is its capacity for sensitization, both by skin contact and by inhalation. Like ethylene amine, a substance used chiefly as an intermediate in the textile industry, which has a similarity of chemical structure but is 40 to 100 times as toxic to animals (Carpenter, Smyth, and Schaffer, 1948), ethylene diamine has been shown to have a systemic injurious effect on animals; by subcutaneous injection (Barbour and Hjort, 1920) and by the oral and respiratory routes its effects are lethal with high dosage. Pozzani and Carpenter (1954) found that inhalation of 1,000 p.p.m. caused death of all the animals within 20 days of the initial exposure with depilation beginning on the sixth day and almost complete after 10 to 15 days. The liver and kidneys showed cloudy swelling, the kidneys some degeneration of the convoluted tubules, and the lungs some congestion. These findings were essentially the same at 500 p.p.m. but at 250 p.p.m. and below there was no significant damage to the internal organs, though there was still some slight depilation. It appears from this work that 132 p.p.m. is the level below which toxic systemic effects do not occur. A marked irritative effect on the eyes of rabbits was observed by Boas-Traube, Dresel, and Dryden (1948), and Smyth (1956) found that liquid ethylene diamine severely injured the cornea.

Blistering of the skin (Boas-Traube *et al.*), dermatitis, respiratory distress, and headache (Dernehl, 1951) have been observed in workmen exposed to ethylene diamine. Dernehl attributed these effects partly to direct irritation, partly to a sensitizing effect. Voluntary inhalation for short periods (5 to 10 seconds) produced slight tingling of the face and irritation of the nasal mucosa at 200 p.p.m. and severe nasal irritation at 400 p.p.m. (Pozzani and Carpenter, 1954). These observers remark that " at any concentration whatever it is to be expected that some previously sensitized persons may develop allergic responses, while the least concentration which can sensitize those not already reactive probably is indefinable ". The threshold limit value for ethylene diamine suggested in 1957 is 10 p.p.m.

Carbon Disulphide

The chronic toxic effects of carbon disulphide have been for many years of greater significance in industry than the acute cerebral effects described. For example, in the Report of the Departmental Committee on Certain Miscellaneous Dangerous Trades in 1899, where it was stated that the windows of a vulcanizing room in one factory had to be barred to prevent men in a state of acute mania from leaping out. Even the well-recognized symptoms of chronic intoxication—polyneuritis, optic neuritis, Parkinson's syndrome, gastro-intestinal disturbances, and psychic changes— are now rarely observed during the course of employment in a process involving the use of carbon disulphide. Descriptions of a late syndrome of vascular origin, however, began to appear from 1942 onwards in the reports of Italian, German, and French investigators. The vascular disturbance appears to be an arterio- or atherosclerotic change in the small arteries of the brain and medulla, giving rise to a diffuse encephalopathic reaction, showing itself as hypertension or nephrosclerosis. According to von Rechenberg (1957), this syndrome, first described by Vigliani and Cazzullo in 1950, as " encephalopathia diffusa sulphocarbonica " appears only after 10 to 15 years' exposure, and once subacute symptoms have appeared is rapidly progressive. The disease has a slow, insidious onset and its development is punctuated by episodes of transient hemiplegia or spastic paresis. The fact that the sufferers are usually under 50 years of age (in a

series of cases described by Vigliani in 1954, the average age was 43) differentiates this form of arteriosclerosis from the ordinary senile form, though the electrocardiogram shows a similar picture. Whether this sclerosis is due to an angiospastic action of carbon disulphide on the arterioles or to an interference with the metabolism of lipoproteins is not yet definitely agreed upon. Vigliani (1954) has suggested that its action might consist of an inhibition of the clearing factor in the blood, thus preventing the transformation of the more coarsely dispersed β-lipoproteins into the finely dispersed α-lipoproteins.

The nephrosclerotic form is accompanied by hypertonia, albuminuria, microhaematuria with casts, and optic disc changes (von Rechenberg, 1957). The actual distribution of the carbon disulphide, which is not eliminated in the expired air or urine, in the various organs and tissues is not at present completely understood nor is it certain whether quantitative determination of very small amounts of CS_2 in the blood will have diagnostic significance in cases of possible chronic poisoning. Such determinations may, however, be of importance in investigating the mechanism of the toxic process, and until recently efforts to find accurate methods, either by extraction or by distillation, have been largely unsatisfactory.

The extraction method described by Hunter in 1940 was based on the formation of a yellow compound, copper diethyldithiocarbamate, when diethylamine and copper acetate were added to a petroleum ether extract of blood, a reaction which has also been used in the estimation of atmospheric concentrations of CS_2 (Sonnenschein and Schäfer, 1953). This reaction formed the basis of an extraction method designed by Bäsing in 1952. He used crystallizable benzene as the extraction agent, and after repeated centrifuging to separate the various layers formed, the diethylamine and copper acetate were added to the benzene layer and the colour reaction determined photometrically by comparison with a known standard. The results showed on the average a loss of only 10% of CS_2.

Distillation methods, attempting to expel the CS_2 from blood and to absorb it in a medium suitable for colorimetric examination, have also been examined by Bäsing (1952) with a view to overcoming the unsatisfactory results of other investigators, and he has devised a method which is claimed to be simple enough to be carried out in factory or clinical laboratories. The absorptive reagent consists of diethylamine, triethanolamine, copper acetate, and ethyl alcohol, which becomes greenish-yellow to brown according to the amount of CS_2 present. It is claimed that by this method very small amounts of CS_2 have been accurately determined in the blood of animals subjected to inhalation.

CONCLUSION

A survey of past and present knowledge of toxic solvents reveals several outstanding features of progress and development in the continuous struggle to preserve the health of workpeople who are exposed to their potential ill-effects, at the same time making full use of the technical and commercial value of those already available and of those constantly being presented to the industrial world.

The first of these features is the ever-growing ability to judge the actual and potential toxicity of any solvent without waiting for the results of trial on the persons working with them. In the early days of rapid expansion in the field of organic solvents this was almost the only method available: if persons using a particular solvent exhibited recognizable symptoms of ill-health, or even died in the absence of accurate diagnosis of their cause, the solvent was judged to be toxic, and measures were instituted to prevent as far as possible the entry of the toxic substances into the body. Nowadays, not only have great advances been made in the problems of construction and installation of machines and in the efficacy of systems of ventilation, but, also, owing to the institution of research laboratories all over the world, it is now possible to forecast by animal experiment whether a solvent is likely to be toxic to human beings and even to determine the probable nature and site of action of its toxic effect. Once these facts are established, even though much deeper research may be needed to translate the effects of animal experiments into human experience, the first steps of prevention can be taken.

The second outstanding feature is the expansion of knowledge of the actual toxic processes within the body by means of the modern instruments of scientific research now available. The fact that metabolic investigations can now be carried out not only on animals but also on exposed human beings has shed a flood of light on the hitherto mysterious problem why one toxic solvent attacks particular organs and tissues, while another, belonging perhaps to the same chemical group, does not. These procedures have opened up the possibility of replacement of extremely toxic substances by others, equally valuable from the technical and economic standpoint but with considerably less harmful and more easily preventable effects on the organism.

A third most valuable advance is the annual publication of those values of atmospheric concentration, based on experimental research and actual human experience, below which persons

engaged for eight hours a day in processes involving exposure to solvents can be expected to suffer no significant or permanent injury to health. By practical application of these values, aided by modern methods of estimating the concentrations in the air of workrooms, even though from time to time it may be found that the recommended values have been placed higher or lower than in the light of further experience they should have been, it is possible to keep the hazard of exposure down to a much lower level than in the days when an unpleasant odour or vague complaints of ill-health were the criteria of too high air concentrations.

Finally, there is still a long way to go before it can be said that any toxic solvent can be rendered entirely innocuous for use by human beings, but the more cases of toxic effects are reported the more will all those who are concerned with the safe use of these valuable tools of industry be able to ensure that their potential for harm to those who use them is minimized to the fullest extent.

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THE OCTOBER (1958) ISSUE

The October (1958) issue contains the following papers:—

Cancer of the Lung and Nose in Nickel Workers. By Richard Doll.

Some Observations on the Incidence of Respiratory Cancer in Nickel Workers. By J. Gwynne Morgan.

The Pathology of the Lungs in Five Nickel Workers. By W. Jones Williams.

Chronic Chloroform Intoxication. By P. J. R. Challen, D. E. Hickish, and Joan Bedford.

Counting Errors due to Overlapping Particles in Thermal Precipitator Samples. By S. A. Roach.

Respiratory Function of Witwatersrand Gold-miners. By Saul Zwi and Margaret R. Becklake.

A Statistical Study of Coal-mining Accidents. By F. D. K. Liddell and Joan May.

Aseptic Necrosis of Bone in Caisson Disease. By John D. Thomson and Andrew B. Young.

Some Notes on the Effects of Excessive Noise on the Hearing of a Group of Workers. By G. F. Keatinge and S. Laner.

An Investigation of Some Health Hazards in an Inert-gas Tungsten-arc Welding-shop. By P. J. R. Challen, D. E. Hickish, and Joan Bedford.

he Estimation of Gaseous Acid in Domestic Premises. By J. J. Phair, R. J. Shephard, G. C. R. Carey, and M. L. Thomson.

Quarry Bank Mill: I. The Story of the Mill. By Robert Murray.

Book Reviews.

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Brit. J. industr. Med., 1959, **16**, 40.

INVESTIGATIONS CONCERNING THE PRE-RADIOLOGICAL STAGE OF SILICOSIS

BY

C. VELICAN, G. LATIS, M. POPA, Gr. POPA, and M. STEINBACH

From the Therapeutics Institute of the R.P.R. Academy, Bucharest

(RECEIVED FOR PUBLICATION DECEMBER 10, 1957)

Twenty-two gold-miners were studied in detail six-monthly for two years after first entering mining. Six men working in the dustiest part of the mine (8,000 to 45,000 particles/ml. all sizes, in rock containing 72% free and combined silica) showed a progressive increase of blood silica, a fall in erythrocytes, and a rise in eosinophils and monocytes. The changes observed were statistically significant only in those exposed to the highest concentrations of dust and occurred before abnormalities were detectable in the chest radiograph.

Several studies have been published since 1930 which demonstrate that silicotic patients exhibit more or less pronounced biochemical and metabolic changes, as well as lesions in many viscera. The systemic features of silicosis are considered to be a consequence of the development of pulmonary lesions, while the clinical picture is considered to be a local and systemic, direct and indirect reflection of the morphological changes occurring within the lungs (Schmid, 1956). Certain authors believe that the constitutional disturbances result from a transition from the compensated, pulmonary form to the decompensated, pleuro-visceral form (Moskovski, 1956).

The existence of an evolutional stage of the disease preceding the onset of the radiological lesions lacks the support of special investigations in this field.

While some investigations have been carried out on the clinical symptoms and functional respiratory tests during the pre-radiological stage of silicosis, we have not come across any longitudinal study, performed over several years in the same group of persons, on alterations in the biochemistry. In our opinion, the need for such investigations seemed all the more important, as we noticed that certain authors consider some of these biochemical changes to be the first sign of the complex disturbances occurring in the course of silicosis. These include more particularly eosinophilia (Rovatti, 1948), increased erythrocyte sedimentation rate (Wiesinger, 1949), altered Na/K ratio (Beckmann and Hilgers, 1957), increased amount of lysozymes and lipoids (Schumacher, 1956), and an increased amount of α_2-globulins and γ globulins in the blood (Timar, 1955).

We have undertaken a follow-up study of the biochemistry and clinical pathology of persons starting work in an atmosphere polluted by various amounts of dust containing silica, as well as of the possible prognostic and prophylactic significance of these changes.

Material and Method

The mine in which our investigations were carried out is formed of rocks of volcanic origin. The seams are formed for the most part of auriferous quartz and of iron and lead sulphides. Free and combined silica in these seams is about 72%.

About 80% of the amount of dust released is due to blasting and the remaining 20% to mucking out. In certain areas the number of dust particles increases to maximum concentrations of 45,000 ml. (all sizes).

About 10% of the total weight of dust is in particles between 0 and 1 μ in diameter, and 50-68% between 1 and 3 μ. In these conditions, one case of silicosis has occurred in less than three years. Apart from this case, the first radiological changes in the pulmonary pattern were noticed after at least five to seven years of exposure to dust (Daniello, 1953). The incidence of the disease was about 10% of the total number of cases under investigation.

These findings enabled us to investigate, at intervals of six months over a period of two years, whether any changes appeared on clinical and laboratory examination before the first changes in the chest radiographs were detected.

The investigations were carried out on 33 subjects, 22 working underground and 11 at the surface in the offices of the plant.

All 33 subjects were aged between 18 and 30 years. They all came from rural areas and had never been exposed to silica dust or toxic gases. None of the subjects had had miners among near relatives.

The 22 underground workers were divided into four groups:

Group A included six men who worked in the areas of maximum dust concentration (from 8,000 to 45,000 particles/ml.) during their whole underground working time. They were miners and miners' assistants.

Group B included persons who worked alternately in the areas of minimum, medium, and maximum dust concentration (from 150 to 30,000 particles/ml.). This group consisted of wagoners.

Group C included persons who worked most of their time underground in areas of minimum dust concentration (from 150 to 500 particles/ml.). This group consisted of technicians, plumbers, engineers, joiners, and sanitary officers.

Group M included persons who worked at the surface, in the offices of the plant, in an atmosphere which was not polluted by dust or gas.

The first clinical and laboratory examinations were carried out during the period preceding the training for underground work. Only those workers in whom all these examinations were normal were selected and followed up after they began working in the mine and inhaling dust containing silica.

The following investigations and determinations were made at six-monthly intervals for two years: physical examination, chest films and radioscopy, electrocardiogram, basal metabolism, blood count and haematocrit, erythrocyte sedimentation rate, blood silica (King's method), blood potassium (Hoffman and Jacobs' method), blood calcium (Clark-Collip's method), ascorbic acid in the blood (Roc and Knether's method), blood cholesterol (Sackett's method), proteinaemia (Hinsberg-Lang's method), silica in the sputum (King's method), and urine analysis.

Results

The correlation coefficient (r) between the increase of blood silica level and the duration of exposure is 0·88 and the regression of blood silica levels on the duration of exposure is given by the equation $y = 0{\cdot}17 \times - 0{\cdot}06$.

TABLE 1

BLOOD SILICA IN GROUP A

Months	0	6	12	18	24
Blood silica (mg./%)	0·24	0·38	0·62	0·82	0·91

Normal values 0·05-0·30 mg. %.

Tables 1 and 2 show that in miners in group A (subjected to a maximum concentration of silica dust) there is a rise of blood silica and in the eosinophil and monocyte counts which is statistically significant. There is also a significant fall in the red cell count.

The differences recorded in the value of other biological indices are not statistically significant in this group nor were there any significant differences in the other groups exposed to less dust.

Discussion

The silica determinations in the blood enabled us to detect, in these rather small groups, what we think is the most interesting and important change that occurs during the pre-radiological stage in potentially silicotic subjects. In the miners who for two years inhaled particles in concentrations varying from 8,000 to 45,000/ml. containing 72% silica, blood silica rose to three or four times the amounts found before exposure. The silica in the blood remained nearly normal in all the other subjects who worked during the same two years in an atmosphere in which dust pollution was slight or absent.

Our observations tend to show that the rise is all the more significant if we consider changes in the individual because the initial level may be lower in some subjects. In maintaining that there is a direct connexion between the degree of dust concentration and the increase of blood silica, we are taking into account not only the results obtained in Group A,

TABLE 2

BLOOD COUNTS AND HAEMATOCRIT IN GROUP A

Months	Erythrocytes (per c.mm.)	Haemoglobin (%)	Colour Index	Leucocytes (per c.mm.)	Segmented Neutrophils (%)	Non-segmented Neutrophils (%)	Eosinophils (%)	Basophils (%)	Lymphocytes (%)	Monocytes (%)	Haematocrit
0	4,066,000	87	0·97	6,800	53	7	1·5	0	29	7·8	41
6	4,270,000	88	0·91	6,980	60	4	2	0	22	12	43
12	4,220,000	84	0·87	6,440	55	1	2	0	30	12	42·5
18	3,870,000	76	0·90	6,500	51	2	5	1	28	13	36
24	3,570,000	70	0·90	5,800	50	2	4·8	0	28	12·8	34
P	<0·01						<0·01			<0·01	

but also those obtained in the other groups. Employees who worked the same number of hours daily, over the same period of two years, with presumably the same variations of the alimentary intake of silica, but in areas in which dust was present in moderate or minimal concentrations, or even absent, do not exhibit this gradual increase in blood silica. The direct relationship existing between blood silica and the dust concentration is also supported by our observations in employees who changed their workplace during the six months' period which separated two examinations. Thus, at the end of one year's work in an area with maximum dustiness, H.A. exhibited an increase of blood silica from 0·15 mg.% before entering the mine to 0·45 mg.%. During the next year, he worked in an only slightly polluted area of the same mine and blood silica dropped to 0·10 mg.%.

Our results are in accord with other published observations (Desoille, Dérobert, Le Breton, Lafuma, and Vacher, 1955; Timar, 1955).

The blood counts in Group A showed an increase in erythrocytes during the first year of underground work, followed by a fall at the end of the second year. This tendency towards an increase in erythrocytes was found in all groups of workers who began underground work, regardless of the concentration of inhaled dust. As a rule, haemoglobin showed similar trends.

The increase in eosinophils and monocytes was almost constantly present in pre-silicotic and silicotic subjects. They can be considered as very early signs in determining prognosis and prophylaxis. In our conditions of investigation they become apparent in potentially silicotic subjects three to five years before the disease could be detected by means of radiological examination.

From our studies we think that the humoral phase of silicosis begins during the second year of exposure to dust, and precedes by three to seven years the radiological phase of the pulmonary localizations. Some of the workers displaying these humoral disorders will in all probability develop no nodular lesions even after inhaling dust for three to seven years and remain only potentially silicotic subjects for a long time. They will only show alterations in biochemistry, a form of clinically and radiologically inapparent silicosis.

We believe that the chief element of the pathogenetic mechanism in the generalization of silicosis is the toxic influence of increased blood silica. This might account for the frequent dissemination of the silica throughout the body with the occurrence of necrotic lesions and connective tissue proliferation in the vascular walls, aorta, myocardium, digestive tract, pancreas, bile ducts, liver, spleen, kidneys, and nervous system. These lesions have also been reproduced experimentally by the parenteral injection of silicic acid. The toxic action of silica upon the adrenals might partly explain the secretory failure reported by certain investigators, which is said to be reflected clinically in the frequent asthenia, adynamism, and anorexia.

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THE DUST CONTENT OF THE LUNGS OF COAL WORKERS FROM CUMBERLAND

BY

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The prevalence of pneumoconiosis varies from one coalfield to another. The present investigation arose from the observation that coal-miners' lungs from west Cumberland appeared much less black and had less coal in them than lungs from South Wales coal-miners.

Dust analyses were carried out on 33 lungs of coal workers from Cumberland which had been examined histologically and graded according to the classification of Belt and King (1945). No case of massive fibrosis (grade 4) occurred and this condition seems to be rare or absent in Cumberland. Compared with South Wales coal-miners' lungs, each histological grade of simple pneumoconiosis was on an average associated with less coal dust and more rock dust in Cumberland, and silicosis due to rock work in coal-mines appeared to be relatively more frequent.

According to certification statistics and direct surveys the prevalence of pneumoconiosis varies from one coalfield to another, and until about 1950 the bulk of the disease in Great Britain was found in the anthracite and steam coal areas of South Wales. A number of lungs from coal workers from these regions have been analysed for their dust content with the general conclusion that the kind of work (rock worker, collier, trimmer) was reflected in the lung dust composition and that increased severity of the disease was associated with increasing amounts of dust (King and Nagelschmidt, 1945; King, Maguire, and Nagelschmidt, 1956).

The present investigation arose from the repeated observations of all three of us on coal-miners' lungs received from west Cumberland that they appeared much less black and on analysis had less coal in them than lungs from South Wales; and the observation of one of us (J.S.F.) that the type of " black lung " characteristic of the advanced stages of pneumoconiosis seen in South Wales (Fig. 4) appeared to be absent in the lungs of coal workers seen at necropsy in west Cumberland. There is believed to be as much dust in the west Cumberland mines as elsewhere, and there appears to be no reason why the coal dust should be inhaled less readily, or eliminated more rapidly, than Welsh coal dust.

Progressive massive fibrosis (P.M.F.) is characterized by a confluent fibrosis, pigmented with carbon, whose origin is considered to be due to chronic infection, frequently, but not invariably, tubercular, superimposed upon a background of simple pneumoconiosis (cf. Cochrane and Miall, 1956). The absence of P.M.F. in Cumberland in contrast with Wales was first observed from 1940 to 1948 when the active interest in coal-miners' pneumoconiosis was developing throughout the various coalfields. At the Cumberland Infirmary, Carlisle, lungs were obtained from coal-miners, (*a*) whose death resulted from accident or natural causes and where no question of compensation for pulmonary disease arose, but whose working lives had been spent as miners, and (*b*) from men to whose death pneumoconiosis was thought to have contributed and consequently post-mortem examinations were ordered by the coroner. The lungs of all these coal-miners were examined during the last 10 years and advanced stages of P.M.F. would have been detected had they existed. There is as much pulmonary tuberculosis in west Cumberland as in Wales and the reports of the County Medical Officer of Health and of the Registrar General reveal that the incidence in certain villages is twice that of England and Wales (Faulds, 1957). The area was scheduled as a depressed area in the early twenties and there was mass unemployment after the general strike. The standard of housing was low and the population has a strong Irish element prone to tuberculous infection (Faulds, 1957).

For these reasons it was considered desirable to analyse a number of lungs to assess the amount and composition of the dust present, and between 1948

FIG. 1.—Cumberland coal-miner's lung: 40 years' exposure; showing only a little coal dust; slight reticulation, Grade 1; No. 3627.

FIG. 2.—Cumberland coal-miner's lung: reticulation and focal emphysema, Grade No. 2; 5648.

FIG. 3.—Cumberland lung: mixed coal and rock dust; focal emphysema, reticulation, and mixed nodulation, Grade 3; No. 4629.

FIG. 4.—South Wales lung, from a case of progressive massive fibrosis (P.M.F.); confluent fibrosis, Grade 4; from King *et al.*, (1956).

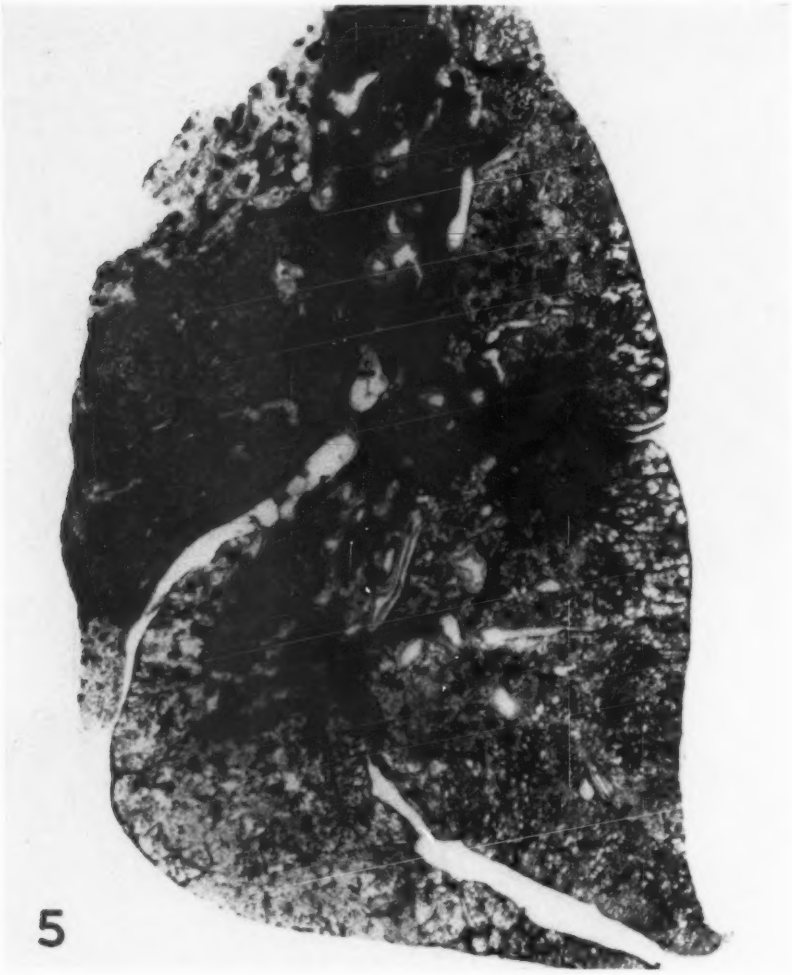

FIG. 5.—Cumberland lung: rock dust and some coal dust; silicotic nodulation; No. 5489.

and 1955 all lungs from men who died in the pits as a result of coronary disease or accident, or who died in hospital, and whose industrial history was known, were retained. Since, in Cumberland, there have been few claims in the past for compensation on account of pneumoconiosis, there were very few radiological examinations made shortly before death, and there was little radiographic evidence of pneumoconiosis for the period covered. Before the National Coal Board took over the mines, accurate records of the types of work undertaken by the workmen during their period of service with the individual pits were not available, and it was therefore difficult to obtain accurate industrial histories in many cases. Also, with the shifting of the population from one pit to another, owing to the exhaustion of the seams, we had frequently to rely on the observations of workmates.

Reasonably accurate histories of work were available in only 33 cases. These form the subject of the present paper. They were classified, according to type of work, into three broad classes, those exposed mainly to rock dust, to mixed dust, and to coal dust. These classes were used because it was often found difficult to assign the men to distinct occupations such as collier, haulier, or rock worker. It may be that in the Cumberland coalfield there is a greater tendency for men to move from one type of work to another in the pit than there is in South Wales.

Experimental

The histological assessments were carried out in sections of blocks taken from several parts of the lung, assisted by large sections which were prepared for us by Professor J. Gough, and the pathological grading was in accordance with that originally described by Belt and King (1945) as modified by Gough (see King *et al.*, 1956), namely, (1) slight reticulation (Fig. 1), (2) reticulation (Fig. 2), (3) mixed nodulation (Fig. 3), (4) confluent fibrosis (Fig. 4), and (5) silicotic nodulation (Fig. 5). The lung dust was isolated and analysed as described previously. Coal was determined from a small sample of dried lung tissue, usually ½ or 1 g., and the mineral (non-coal) residue was isolated from a larger sample, usually 50 g. Total silica was determined chemically and the quartz content by a quantitative *x*-ray diffraction technique (Gordon and Harris, 1956). Apart from quartz, mica was the main constituent of the mineral fraction, and kaolin was found in minor amounts in many but not all of the residues. The total lung weight was available in 27 of the 33 cases.

The lungs examined are classified in Table 1 according to dust exposure and pathological grading. Half the cases showed grade 2, but grade 4 (confluent fibrosis) was absent. This is in strong contrast to the distribution seen in necropsy material in Cardiff (Gough, 1954) where between 1946 and 1948 only about one-fifth of all lungs showed grade 2 and half the material was of grade 4, *i.e.*, confluent fibrosis. Although statistically neither source is a satisfactory one for assessing the relative prevalence of the various grades of disease the difference between the two regions is nevertheless very striking.

TABLE 1

NUMBER OF LUNGS IN DIFFERENT PATHOLOGICAL GRADES AND DUST EXPOSURE CLASSES

Dust Exposure Class	Pathological Grade					No. of Men	Mean Pathological Grade
	1	2	3	4	5		
Mainly rock dust	—	—	—	—	2	2	5
Mainly mixed dust	2	2	3	—	4	11	3·2
Mainly coal dust	4	14	2	—	—	20	1·9
Totals	6	16	5	—	6	33	

Results

The data are given fully in Table 2, where for each of the three dust exposure classes the lungs are given in increasing grades of pathology and, within each grade, in increasing amounts of total dust expressed as percentage of the dried lung.

Grade 1 lungs, *i.e.*, slight reticulation, showed no more discoloration than those of a city dweller, and histologically there were minute dust foci surrounded by microscopic emphysema. These foci resembled spiders' webs, with a central zone composed of

TABLE 2

DUST CONTENT OF LUNGS OF COAL WORKERS FROM CUMBERLAND

Dust Exposure Classes	Necropsy Number	Age	Exposure (years)	Pathological Grade	Percentage Dried Lung					Weight of Dried Lung (g.)	Total Estimated Dust in Both Lungs (g.)	Ratio: Coal / Sil. Min	Quartz as % of Total Lung Dust
					Total Dust	Coal	Sil. Min.*	Quartz	SiO_2				
I	6001	73	52	5	7·28	1·05	6·23	1·0	3·6	130	19	0·17	14
Rock dust	5920	75	40	5	15·05	1·62	13·43	2·42	7·3	188	57	0·12	16
II	5983	51	20	1	0·81	0·71	0·10	0·01	0·05	170	2·75	7·1	2
Mixed dust	5496	74	30	1	1·92	1·00	0·92	0·1	0·40	119	4·6	1·1	5
	6161	59	45	2	3·20	1·78	1·42	0·23	0·79	178	11·4	1·2	7
	4214	47	32	2	13·5	5·8	7·7	0·85	4·2	170	46	0·75	6
	4629	58	40	3	2·44	1·34	1·10	0·28	0·69	86	4·2	1·2	11
	4473	40	23	3	4·01	1·1	2·91	0·44	1·53	—	—†	0·38	11
	4409	68	31	3	7·87	4·44	3·43	0·51	1·81	—	—†	1·3	6
	6169	57	30	5	4·97	3·08	1·89	0·98	1·3	—	—†	1·6	20
	5489	45	27	5	5·23	0·42	4·81	0·96	2·64	200	21	0·1	18
	4274	61	24	5	5·30	0·84	4·46	1·5	3·0	—	—	0·2	20
	5980	56	32	5	6·61	1·06	5·55	1·11	3·3	97	12·8	0·19	17
III	4829	46	31	1	0·7	0·44	0·25	0·02	0·14	103	1·4	1·8	3
Coal dust	3627	67	40	1	2·67	1·26	1·41	0·16	0·77	—	—†	0·9	6
	5987	75	40	1	3·74	3·10	0·64	0·07	0·35	62	4·6	4·9	2
	6181	48	—	1	4·01	2·70	1·31	0·12	0·60	119	9·5	2·06	3
	5412	47	33	2	0·82	0·52	0·30	0·04	0·16	107	1·8	1·75	5
	5053	45	30	2	1·22	0·49	0·73	0·13	0·42	158	3·8	0·67	11
	5695	62	41	2	1·50	0·64	0·86	0·10	0·47	55	1·7	1·74	7
	5014	35	21	2	1·69	0·77	0·92	0·07	0·50	134	4·6	0·84	4
	5088	73	48	2	2·28	0·94	1·34	0·15	0·73	88	4·0	0·70	6
	6178	67	—	2	2·86	1·37	1·49	0·16	0·71	106	6·0	0·9	6
	5648	71	—	2	3·07	1·14	1·93	0·29	1·04	150	9·0	0·6	9
	6065	54	41	2	3·24	2·68	0·56	0·09	0·32	201	13·0	4·8	3
	6094	57	—	2	3·37	1·35	2·02	0·24	1·04	160	11·0	0·7	7
	4115	70	50	2	3·5	1·63	1·87	0·21	1·12	132	9·2	0·87	6
	5981	55	40	2	3·78	2·64	1·14	0·16	0·60	—	—†	2·3	4
	5885	50	35	2	5·60	3·38	2·22	0·22	1·18	92	10·3	1·5	4
	4428	59	33	2	7·16	3·0	4·16	0·25	1·45	128	18·3	0·72	3
	4148	62	49	2	9·64	7·98	1·66	0·46	0·08	73	14·0	4·8	5
	5761	65	—	3	7·68	4·31	3·37	0·54	1·84	102	16·0	1·3	7
	4865	42	27	3	9·4	7·56	1·84	0·17	1·10	98	18·6	4·1	2

* Siliceous minerals. *i.e.*, the sum of kaolin, mica, and quartz. †Not determined; only part of lung available.

dust-laden macrophages in varying degrees of disintegration, and thickened alveolar walls radiating out from the focus. The dust foci, usually associated with peribronchial and perivascular lymphatics, were scattered generally throughout the lung, but were more numerous in the upper lobes and upper part of the lower lobes. Grade 2 resembled grade 1, but with a greater concentration of the dust foci and more emphysema. The emphysematous areas were generally larger and more prominent.

The five lungs of the present series belonging to grade 3 fell into two different classes and the histological picture reflected the different nature of dust to which they had been exposed. Necropsies Nos. 4865 and 5761 (see Table 2) were of men who had worked mainly in coal dust. The fibrosis was more diffuse, less dense and hyaline, and there was little nodulation. The coal dust was collected into small areas with distinct emphysematous bullae easily recognized by the naked eye. In these two cases there was no histological evidence of tubercle. In the other three, Nos. 4409, 4473, and 4629, all of whom had worked in mixed dust, the reticulation had microscopic nodulation. These nodules, 0·5 mm. to 3·0 mm. in diameter, were composed of hyaline fibrous tissue and had no condensed edge, but tended to coalesce into larger masses. The amount of carbon pigmentation was smaller microscopically than in the former two cases and quartz crystals could be demonstrated more easily. In two of these three cases there was histological evidence of a terminal tuberculous infection. The lung dust analyses confirmed the histological findings except for necropsy No. 5761 which had a higher quartz content than would have been expected.

There were no cases of massive fibrosis, and the cases classified as grade 5 showed the characteristic picture of nodular silicosis with collagenous nodules relatively free from coal dust.

The analytical data are set out in the same way as previously (King *et al.*, 1956), but quartz as a percentage of total lung dust has been added in view of the apparently more important role it occupies as a factor in causing lung disease in Cumberland coal workers.

Mean results for the exposure classes are given in Table 3A. The two rock workers, who had both been master drifters, showed significantly more rock dust and more quartz when expressed as a percentage of dried lung than either of the other two groups, and the same criteria distinguished the mixed dust from the pure coal dust group. This confirms that the grouping was reasonable; it had been based on the environmental histories before the analytical work was started.

The differences for the pathological grades are shown in Table 4A, and results, expressed in grams of the different dust constituents in both lungs, are compared with data from South Wales (King *et al.*, 1956) in Fig. 6.

With the increase of the pathological grade, a corresponding increase in the amount of dust was observed; as Table 4B shows, these increases were not significant when comparing each grade with the next one, but the differences between grades 3 and 1 were significant at the 2% level for total dust, at

TABLE 3A

DUST CONTENT FOR DIFFERENT DUST EXPOSURE CLASSES

Type of Dust	Number of Men	Mean Dust Exposure (years)	Percentage Dried Lung				Total Estimated Dust in Both Lungs (g.)
			Total Dust	Coal	Sil. Min.	Quartz	
Rock	2	46	11·2 (3·9)	1·3 (0·3)	9·8 (3·6)	1·71 (0·71)	38 (19)
Mixed	11	30	5·1 (1·0)	2·0 (0·5)	3·1 (0·7)	0·63 (0·15)	14·7* (5·8)
Coal	20	37	3·9 (0·7)	2·4 (0·6)	1·5 (0·2)	0·18 (0·05)	7·8† (1·6)

Figures in brackets are standard errors of means. *Based on seven lungs. †Based on 18 lungs.

TABLE 3B

SIGNIFICANCE LEVELS OF DIFFERENCES OF MEAN VALUES IN TABLE 3A

Differences of Occupational Dust Exposures	Significance Level (%) for:				
	Percentage Dried Lung				Total Estimated Dust in Both Lungs (g.)
	Total Dust	Coal	Sil. Min.	Quartz	
Rock dust minus mixed dust	10	NS	1	5	NS
Rock dust minus coal dust	1	NS	0·1	0·1	0·1
Mixed dust minus coal dust	NS	NS	1	1	NS

NS = not significant.

TABLE 4A

DUST CONTENT OF LUNGS FOR VARIOUS PATHOLOGICAL GRADES

Pathological Grade	Number of Men	Mean Dust Exposure (years)	Percentage Dried Lung				Total Estimated Dust in Both Lungs (g.)
			Total Dust	Coal	Sil. Min.	Quartz	
1	6	32	2·31 (0·6)	1·54 (0·4)	0·77 (0·2)	0·08 (0·02)	4·6*
2	16	36	4·15 (0·8)	2·26 (0·5)	1·89 (0·4)	0·23 (0·05)	10·9†
3	5	30	6·28 (1·3)	3·75 (1·2)	2·53 (0·5)	0·39 (0·07)	12·9‡
5	6	32	7·41 (1·6)	1·34 (0·4)	6·06 (1·6)	1·33 (0·23)	27·4§

Figures in brackets are standard errors of means. *Based on five lungs. †Based on 15 lungs. ‡Based on three lungs. §Based on four lungs.

TABLE 4B

SIGNIFICANCE LEVELS OF DIFFERENCES OF MEAN VALUES GIVEN IN TABLE 4A

Differences of Pathological Grades	Significance Level (%) for:				
	Percentage Dried Lung				Total Estimated Dust in Both Lungs (g.)
	Total Dust	Coal	Sil. Min.	Quartz	
2 — 1	NS	NS	NS	10	NS
3 — 1	2	10	1	0·1	10
3 — 2	NS	NS	NS	NS	NS

NS = not significant.

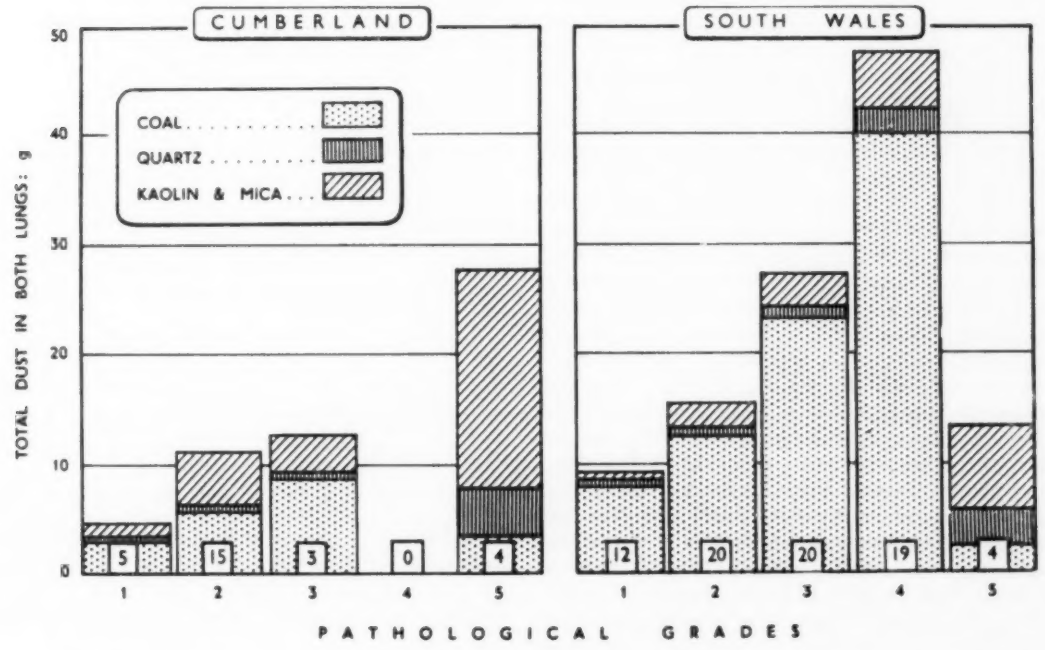

FIG. 6.—Dust content of coal-miners' lungs of different pathological grades. (The numbers in squares show how many cases of each grade were examined.)

the 1% level for rock dust, and at the 0·1% level for quartz. In other words, the more dust there was, and especially the more rock dust and quartz, the more advanced was the fibrosis. The average quartz content of the total lung dust in each grade ranged from 19% for the silicosis grade to 3·4% in grade 1, but only in grade 3 was it significantly higher than in comparable lungs from South Wales, as shown in Table 5. On the other hand, the total dust in

TABLE 5

QUARTZ AS PERCENTAGE TOTAL LUNG DUST IN CUMBERLAND AND SOUTH WALES

Pathological Grade	1	2	3	4	5
Cumberland	3·4 (6)	5·8 (16)	7·4 (5)	—	19 (6)
South Wales*	3·9 (11)	5·2 (20)	4·6 (20)	4·1 (19)	23 (4)

Figures in brackets are number of lungs in the different groups.
*From King *et al.* (1956), Table 7, excluding the tin miners and including, for grade 5, data from King and Nagelschmidt (1945).

pathological grades 1, 2, and 3 for South Wales was about double that for Cumberland, while the proportion of dusts other than coal was lower (Fig. 6).

Comment

The composition of dust in the lungs of coal workers with pneumoconiosis in Cumberland shows a broad similarity to that found in the South Wales miners. The same minerals occur, but the amounts of dust are less in the early stages of disease, and the proportion of stone dust is greater and that of coal smaller. Relatively more cases of silicosis are seen at necropsy, and rock dust appears to be comparatively more important in Cumberland than in South Wales in the production of lung pathology. Cases of P.M.F. do not exist or are very rare. The simplest reason for this would be that the men in South Wales were exposed to more respirable dust than those in Cumberland. Mine ventilation in Cumberland was probably better on an average, and the men tended to go to the coalface, where dust concentrations are highest, at a later age than Welsh miners. This effect has been shown to correspond to a shift of about 10 years in the curve relating pneumoconiosis prevalence to dust exposure, when comparing Durham with South Wales coal-miners (McCallum and Browne, 1955). Against this, mechanical cutting advanced earlier in Cumberland (Ministry of Fuel and Power, 1945, Table 1), and increasing mechanization tends to cause higher dust concentrations. It will probably never be possible to know with any degree of accuracy whether between 1920 and 1950, when the bulk of disease with which we are concerned was produced, Cumberland coal-mines were less dusty than Welsh anthracite or steam coal-mines.

It is conceivable that there are factors connected with the type of coal which could cause the difference in amount of pneumoconiosis. Coal from Cumberland, which contains much volatile matter, could be less prone to accumulate in the lungs than anthracite and steam coal, which have a lower volatile content, if Cumberland coal is taken up more readily by phagocytes and removed through coughing and swallowing the dust. Animal experiments by injection technique, in which Welsh anthracite and Cumberland coal were compared, failed to give any clear difference in recoveries of these coals from the lungs up to eight to 12 months after injection (Nagelschmidt, Nelson, King, Attygalle, and Yoganathan, 1957), but it could be argued that the injection technique, which introduces massive amounts of dust suddenly into the lungs, is unsuitable to demonstrate this effect. Further research would be required to settle the point. This is in progress, but to date there is no evidence we know of to indicate that one kind of coal dust may be more rapidly eliminated from the lung than another, or against whose access the lung may possess a better barrier. Unless such a difference can be demonstrated between Welsh and Cumberland coal dust, it is probable that the differences in the coal contents of lungs of miners from the two areas are due to lower dust exposures.

Thanks are due to Professor J. Gough for providing the large sections, to Mr. B. A. Maguire for the statistical analyses, and to Misses R. Paul, E. S. Nelson, and J. Vincent for analytical help. One of us (E.J.K.) would like to thank the Medical Research Council and the National Coal Board for financial assistance. This paper is published by permission of the Ministry of Power.

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RESPIRATORY FUNCTION AND DISEASE AMONG WORKERS IN ALKALINE DUSTS*

BY

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Little is known of the possible effects of sodium carbonate dust on the lower respiratory passages. A large alkali industry, with a number of works, was used for an investigation of lime and soda ash dusts evolved during the process. The physical and chemical characteristics of these dusts and details of the type of work and environmental conditions are described. In 1954 and 1956 a survey was made of respiratory sickness absence, chest radiographic appearance, and respiratory function in workers employed in areas with exposure to soda ash, lime dust, and no dust. All were interrogated about their smoking habits. In 1954 there was found to be a significant reduction in expiratory flow rate of workers in dusty jobs in soda ash compared with the group not exposed to dust but this result was nullified in a random sample group in 1955 and in full groups in 1956. Respiratory sickness absence was found to be slightly greater in workers in dusty occupations, particularly in lime dust. No pneumoconiosis was detected on miniature films. The survey of smoking habits revealed that smoking was associated with a definite decrease in the expiratory flow rate, particularly after the age of 40 in heavy smokers. It was concluded that smoking habits played a more important part than alkaline dusts in the reduction of respiratory efficiency as measured by a study of sickness absence and performance of a simple spirometric test.

The irritant effect of sodium carbonate dust on the nasal mucous membrane was shown by Archibald (1954). Chronic inflammatory disease of the larynx from exposure to this dust was found by Profazio and Troisi (1953). However, no reports have been published on the possible effects of sodium carbonate dust or soda ash on the lower respiratory passages. Soda ash might be expected to produce a reaction on the mucous membranes of the lower respiratory tract. Despite the filtering action of the nasal cilia, small particles are likely to adhere to the walls of the bronchi, or indeed, enter the alveoli. Soda ash in aqueous solution is strongly alkaline (*p*H 11·6 to 12) and as the ciliated columnar-celled mucous membrane of the bronchi is identical with that of the larynx, a chemical inflammation might well result. Lime, being both alkaline and, when burnt, soluble, should produce a like effect. Doig (1955) found eight cases of pneumoconiosis in limestone workers who had been exposed to mixed dust containing silica. Although considered to be due to limestone these cases were primarily of silicosis. Bridge Davis and Nagelschmidt (1956) carried out clinical and radiographic examinations of 14 men who had worked in pure limestone for periods varying from 12 to 35 years; no evidence of pneumoconiosis was found although the dust counts showed many thousands of particles between 0·5 and 5 μ in the atmosphere to which the men were exposed. Raymond *et al.* (1952) in 41 limestone quarrymen found no evidence of respiratory disability, though chronic bronchitis and emphysema were recorded. Cement, which is calcined limestone, was investigated by Gardner, Durkan, Brumfiel, and Sampson (1939) and no disability was found in workers exposed to dust in the grinding process. Sander (1958) surveyed again 195 cement workers who had been included in Gardner's original survey and who had had from 20 to 45 years of exposure to cement dust. There were minor changes (" linear exaggeration ") in the chest radiographs of those exposed to raw or mixed cement dust, but in those exposed to finished cement dust alone there were no recognizable changes in the chest radiographs even after upwards of 30 years' exposure. Symptomless perforation of the nasal septum in cement workers was found by Marchand (1944). Hunter

* This paper is an abridged version of the essay which won the Occupational Health Prize of the British Medical Association, 1957.

(1955) mentions harmless arborescent markings in chest radiographs of workers in limestone quarries.

The Registrar General's Decennial Supplement on Occupational Mortality (1931) gave the standardized mortality ratio (S.M.R.) for chemical workers as 80. In the 1951 Supplement the S.M.R. for chemical workers is given as 85. An analysis of the mean annual death rate from all causes per 100,000 and the ratio of death rate to that of all males taken as 100 indicates that chemical workers of all ages, except 70 to 75, have a relatively favourable mortality. No mortality data specific to the alkali industry are available. Respiratory mortality was lower in chemical workers than in other workers generally.

These studies on the two dusts which are most prevalent in the mid-Cheshire alkali industry suggested the need for an enquiry into the functioning of the lower respiratory tract of workers exposed to these dusts, and the possible existence of any unusual or excessive morbidity attributable to them.

Type of Works

The mid-Cheshire alkali industry is largely carried on in four works: one large (A); two medium-sized (B) and (C); and one small (D). Works A, B, and C are within one mile of a town of 35,000 inhabitants which has no other major industry. Works D is in open country three miles from the town. The approximate total numbers employed are:

Works	Approximate No. of Pay Roll Workers	Dusts Involved in Process
A	2,500	Lime
B	1,000	Ash and lime
C	700	Ash and lime
D	200	Nil

These numbers include all employees on the pay roll. Thus the men under consideration, namely those continually exposed to the dust in certain areas in the works A, B, and C, were only a small proportion of the total (Table 1).

At works A caustic soda and its by-products and at works B and C sodium carbonate and its by-products are made. The three alkali works (A, B, and C) produced lime dust, either as limestone or burnt lime, and sodium carbonate dust as a result of part of the process. At works D where brine is won through holes in the earth, there is no dust and the workers here therefore served as controls.

Type of Work

Soda ash manufacture has been carried out for over 75 years and caustic soda manufacture for over 40 years in this district. The three raw materials (brine, limestone, and coke) are used in a chemical reaction with ammonia (derived from gas works crude liquor) to produce sodium bicarbonate. This is calcined to produce sodium carbonate (soda ash) or reacted with lime to produce caustic soda. No fundamental alterations in this industry have occurred since it started and the only changes in the exposure of men to the dusts under consideration have been a gradual reduction in the evolution of dust and a better extraction of the dust which found its way into the atmosphere.

The process is continuous and therefore all workers on it have to work on a shift rota, whereas those handling the finished product or raw materials need only work by day. The workmen in the lime areas at works A, B, and C work three shifts and their job is to despatch from stock quantities of limestone (calcium carbonate) to the kilns where it is burned with coke to form burnt lime (calcium oxide) and to dissolve the burnt lime to form milk of lime (calcium hydroxide). At the times during the shift when lime and limestone are conveyed on bands, the atmosphere in the kilns where the men are working is noticeably dusty. The lime bands run during all the shift except for half an hour, and the limestone band runs for two to three hours per shift. Little, if any, dust comes from the coke which is added in small quantities to the limestone at an early stage.

Workers in soda ash may be divided into two groups. One deals with the packing and loading of 1 to 2 cwt. bags of soda ash. The second reclaims jute bags which have been soiled and caked with soda ash. Physical demands are greater in both these groups than in those on process work and dust exposure is both heavy and prolonged. Many of the men employed in the soda ash areas, the bag packers, bag stitchers, and handlers of contaminated bags, do not move about much during their work; the concentration of dust inhaled is thus greater and more constant than in the lime area.

Works D is mainly concerned with the erection, maintenance, and working of brine boreholes. The erection and maintenance is done by day workers, but approximately 20 shiftmen are needed to look after the bore holes at night. Physical fitness is needed, as much of the work involves the use of weighty tackle and there is very little protection from weather.

Dusts Produced

The dusts are chemically of two groups: lime (calcium carbonate and oxide) and soda ash (sodium carbonate). All of them are white, flocculent and anhydrous. The alkalinities of the dusts are:

Lime { calcium carbonate (limestone) *p*H 8·5
calcium oxide (burnt lime) *p*H 12·5
Soda ash (sodium carbonate) *p*H 11·6 to 12·0

The varieties of soda ash (light, dense, and granular) are chemically identical but vary in structure. The dusts at the various sampling places are microscopically similar.

Chemical analysis revealed that the silica content of limestone varied from 0·35 to 0·42% at the different works and was approximately 2·8% when the limestone was burned to produce calcium oxide. Soda ash contained no silica.

Method of Survey

Selection of Test Method.—Simple tests of respiratory function have been used in the assessment of disability in pneumoconiosis for a number of years. Garrad (1949) using the vital capacity, investigated Cornish tin-miners. More modern tests, including the maximum breathing capacity test and gas distribution and transfer estimations, have been utilized by Motley, Lang, and Gordon (1949) and Gilson, Hugh-Jones, Oldham, and Meade (1955) on miners with varying degrees of disability. Kazantzis and Buxton (1956) used the maximum breathing capacity test (M.B.C.) and both the conventional vital capacity and the expiratory fast vital capacity tests in a survey of the respiratory function of men casting cadmium alloys.

The test described by Kennedy (1953), using a graphic method of recording a tracing on a moving drum, is short and simple and needs little effort or cooperation on the part of the subject. The expiratory flow rate at 40 breaths/min., *i.e.*, "the timed vital capacity" or "expiratory fast vital capacity" (E.F.R.) showed a correlation of +0·927 with the maximum breathing capacity. The standard error of 5·95 l./min. on single tracings, compared with a mean of 2·43 l./min. averaged over six tracings, indicated a high degree of reproducibility. This test was therefore adopted.

Every effort was made to obtain as many volunteers as possible for the respiratory tests but nevertheless the lapse rate was regrettably high. The morbidity and radiographic findings were not obtained directly from the men, though their cooperation was required in filling up the questionnaire on smoking. The men who were on incentive bonus were given the assurance of the management that no loss of pay would result from time spent away from work while undergoing tests. The tests were undertaken at the most convenient time of day and at a site near the work. As only a very small number of employees working in soda ash and lime are women (approximately 20) only men were included in the investigation. All volunteers, between 20 and 70 years of age, were allowed to undergo the test, though some of them were known to have respiratory disabilities of long standing.

Many of the volunteers for the respiratory function test also volunteered for a routine mass miniature radiograph (M.M.R.) at works A. No pneumoconiosis was found, but simple pneumoconiosis cannot, of course, be detected with reliability on small films.

Lapsed Volunteers

Table 1 shows the number of volunteers and lapsed employees in 1954 together with the total possible in each exposure group. Certain results were inconsistent and in 1956 all employees in the designated areas were therefore again encouraged to volunteer. Table 2 shows the distribution of the 1956 group; the lapse rate was unfortunately high.

The average age in both volunteers and lapsed groups (Table 3) shows slight variability except in the 1954 "no-dust lapsed group", which is markedly high because of the inclusion of nine men over the age of 60*.

* (1) The differences shown in numbers of attacks per man are not large enough to prove any systematic difference between the lapsed and volunteer groups.

(2) There is no evidence that the number of weeks' absence per attack differs amongst the groups, though there is a significant fall between 1954 and 1956. This taken in conjunction with (1) above, makes it unlikely that the changes in weeks of absence per man shown in Table 4 represent a genuine effect.

TABLE 1

DISTRIBUTION OF VOLUNTEERS AND LAPSED EMPLOYEES IN 1954

Exposure Group	No. Possible	Volunteers	% Volunteered	No. Lapsed	% Lapsed
No dust	218	188	86·24	30	13·76
Lime	197	134	68·03	63	31·97
Soda ash	305	243	79·68	62	20·32
Total	720	565	78·47	155	21·53

TABLE 2

DISTRIBUTION OF VOLUNTEERS AND LAPSED EMPLOYEES IN 1956

Exposure Group	No. Possible (1954 Volunteers)	Volunteers 1956 (from 1954 Volunteers)	% Volunteered	No. Lapsed	% Lapsed	1956 New Volunteers	Total Volunteers
No dust	188	89	47·34	99	52·66	37	126
Lime	134	83	61·95	51	38·05	25	108
Soda ash	243	167	68·72	76	31·28	62	229
Total	565	339	60·00	226	40·67	124	463

TABLE 3

COMPARISON OF AVERAGE AGES OF VOLUNTEER AND LAPSED GROUPS IN 1954 AND 1956

Exposure Group	1954				1956			
	No. of Volunteers	Average Age	No. Lapsed	Average Age	No. of Volunteers	Average Age	No. Lapsed	Average Age
No dust	188	43·8	30	50·8	89	42·6	69	45·9
Lime	134	43·5	63	45·0	83	44·3	49	41·6
Soda ash	243	41·2	62	43·8	167	41·2	52	42·3

Examination of the sickness absence of the 1954 and 1956 groups shows that the " no-dust lapsed " subjects had a higher attack and sickness duration rate than other groups. The nine men aged 60 and over in the no-dust lapsed group contributed 17 attacks and 90 weeks lost. This will have materially affected the results. However, there appears from Table 4 to be no significant difference between the lapsed and volunteer groups in lime and soda ash works.

TABLE 4

TOTAL RESPIRATORY SICKNESS ABSENCE AS WEEKS LOST AND ATTACK RATE PER MAN OF VOLUNTEER AND LAPSED GROUPS IN 1954

Exposure Group	Lapsed Group		Volunteer Group	
	Attacks per Man	Weeks Lost per Man	Attacks per Man	Weeks Lost per Man
No dust	1·07	4·73	0·505	1·65
Lime	0·73	2·55	0·619	1·55
Soda ash	0·5	1·43	0·531	1·38

In 1956 examination of the sickness absence of the lapsed group shows that this is very similar both for attack and sickness duration rate compared with the volunteer group, though the volunteer lime group was higher than the others (Table 5).

TABLE 5

TOTAL RESPIRATORY SICKNESS ABSENCE AND ATTACK RATE PER MAN OF VOLUNTEER AND LAPSED GROUPS IN 1956

Exposure Group	Lapsed Group		Volunteer Group	
	Attacks per Man	Weeks Lost per Man	Attacks per Man	Weeks Lost per Man
No dust	0·56	1·71	0·507	1·56
Lime	0·53	1·43	1·10	2·21
Soda ash	0·69	2·13	0·611	1·39

Evaluation of Sample

The workers in soda ash from works B and C and workers in lime from works A, B, and C were the two dust groups which were to be compared with those from control works D, which had no dust. Table 6 shows that these groups were similar in age and physique.

In 1956 the sample was obtained as before and the same volunteers and any others were asked to attend.

TABLE 6

MEAN AGE, HEIGHT, AND WEIGHT OF THE THREE GROUPS IN 1954

Exposure Group	No.	Mean Age (yr.)	Height (in.)	Weight (lb.)
No dust	188	43·89	68·02	155·2
Lime	134	43·46	67·99	149·5
Soda ash	243	41·19	68·17	150·5

The numbers and mean ages of those who volunteered in 1956 are shown in Table 7.

TABLE 7

MEAN AGE OF THREE GROUPS IN 1956

Exposure Group	No.	Mean Age (yr.)
No dust	126	42·5
Lime	108	45·5
Soda ash	229	42·8

Test Methods

Industrial History.—Note was made of a number of characteristics, *e.g.*, age, height, weight, and smoking habits, of each volunteer at the time of the test.

The type of exposure, whether to soda ash, lime, or no dust was also noted. The duration of years of exposure to each dusty or non-dusty atmosphere was recorded. As all men were coded for these works the exposure can be considered pure.

Physiological Test.—A minimum rest period of two to three minutes was allowed. Where any obvious dyspnoea or cough was present before the test, the subject waited until the breathing had returned to normal or the cough ceased.

The apparatus used was a simple spirometer with a constant speed kymograph. The subject was seated facing the spirometer but unable to see the tracings on the drum. After the subject had taken a deep breath he blew strongly through the mouthpiece. Using a protractor and carriage, the vital capacity and the expiratory flow rate were calculated. The average of the best three and the best result were recorded for both the vital capacity and the expiratory flow rate. The volumes were corrected to standard temperature and pressure.

Sickness Absence.—The names of employees certified sick by their own doctors were sent via the labour departments to the health visitors. The health visitors' records were used whenever possible in order to obtain a precise diagnosis; when not available the labour department records were used. In this way all employees'

TABLE 8

AGE AND DURATION OF EXPOSURE OF THE EMPLOYEES IN THE THREE GROUPS IN 1954

Exposure (Years)	No Dust					Lime					Soda Ash				
	Age Groups					Age Groups					Age Groups				
	20–	30–	40–	50–	60–	20–	30–	40–	50–	60–	20–	30–	40–	50–	60–
6–	40	31	36	20	3	11	49	28	11	1	40	71	38	13	1
11–	—	—	12	25	8	—	1	7	7	1	6	6	14	12	2
21–	—	—	—	2	5	—	—	2	7	2	—	1	9	15	4
31–	—	—	1	3	—	—	—	—	2	3	—	—	1	5	2
41–	—	—	—	1	1	—	—	—	1	1	—	—	—	1	2

TABLE 9

AGE AND DURATION OF EXPOSURE OF THE EMPLOYEES IN THE THREE GROUPS IN 1956

Exposure (Years)	No Dust					Lime					Soda Ash				
	Age Groups					Age Groups					Age Groups				
	20–	30–	40–	50–	60–	20–	30–	40–	50–	60–	20–	30–	40–	50–	60–
6–	23	29	22	24	—	3	31	30	6	2	17	73	33	15	4
11–	1	—	2	11	2	—	—	5	10	2	2	17	16	10	3
21–	—	—	2	3	4	—	—	1	7	4	—	1	6	16	5
31–	—	—	—	1	2	—	—	—	1	4	—	—	1	6	—
41–	—	—	—	—	—	—	—	—	—	2	—	—	—	1	3

health records were obtained. The diagnoses were coded in accordance with the International Statistical Classification of Diseases. Hughes (1952) used this classification to indicate subgroups and two of his subgroups (upper and lower respiratory illness) were used for differentiation. Thus, the number of attacks and total weeks lost for each employee were ascertained.

Results

Industrial Dust Conditions.—The duration of exposure of the three exposure groups is shown in Tables 8 and 9. The concentrations of dust were determined by collecting the dust from a measured volume of air on a filter paper. The gradings of the dusts were measured by microscope counts on samples collected, on an electrostatic precipitator (Table 10). Representative points for dust collection were chosen. Most of the workers were placed in constant concentrations of lime dust and a central point was therefore chosen. Ash workers may be exposed to high or low concentrations depending on their work, and therefore both figures were noted. The advantageous effect of a good exhaust system is shown by the figures which do not indicate a high percentage of small particles.

TABLE 10

REPRESENTATIVE DUST PARTICLE CONCENTRATIONS IN COMPARABLE WORKING PLACES

Works		Average Dust Concentration ($\frac{mg.}{m^3}$)	Number of Particles Less than 4·5 μ per cu. ft./air	Particles Less than 4·5 μ (% by weight)
Lime:	A	8·82*	2,780	0·018
	C	2·1	662	
Soda Ash:	B	184·5 max.*	745,000	
		4·9 min.	19,800	0·215
	C	50·3 max.	203,000	
		2·1 min.	8,500	
No Dust:	D	0·3	89	0·017

* The concentration was much reduced later by dust extraction equipment already present at works C.

Sickness Absence.—Table 11 shows the sickness experience in contrasted dust exposure groups.

There were no significant differences between exposure groups in the mean frequency and time

TABLE 11

MEAN FREQUENCY AND TIME LOSS IN 1954

	No Dust Group			Lime			Soda Ash		
	Total No. in Groups	Attacks per Man	Weeks Lost/Man	Total No. in Groups	Attacks per Man	Weeks Lost/Man	Total No. in Groups	Attacks per Man	Weeks Lost/Man
Upper respiratory illness	188	0·505	1·65	134	0·619	1·552	243	0·531	1·38
Lower respiratory illness	188	0·181	0·856	134	0·164	0·604	243	0·152	0·514

TABLE 3

COMPARISON OF AVERAGE AGES OF VOLUNTEER AND LAPSED GROUPS IN 1954 AND 1956

Exposure Group	1954				1956			
	No. of Volunteers	Average Age	No. Lapsed	Average Age	No. of Volunteers	Average Age	No. Lapsed	Average Age
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Examination of the sickness absence of the 1954 and 1956 groups shows that the " no-dust lapsed " subjects had a higher attack and sickness duration rate than other groups. The nine men aged 60 and over in the no-dust lapsed group contributed 17 attacks and 90 weeks lost. This will have materially affected the results. However, there appears from Table 4 to be no significant difference between the lapsed and volunteer groups in lime and soda ash works.

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The type of exposure, whether to soda ash, lime, or no dust was also noted. The duration of years of exposure to each dusty or non-dusty atmosphere was recorded. As all men were coded for these works the exposure can be considered pure.

Physiological Test.—A minimum rest period of two to three minutes was allowed. Where any obvious dyspnoea or cough was present before the test, the subject waited until the breathing had returned to normal or the cough ceased.

The apparatus used was a simple spirometer with a constant speed kymograph. The subject was seated facing the spirometer but unable to see the tracings on the drum. After the subject had taken a deep breath he blew strongly through the mouthpiece. Using a protractor and carriage, the vital capacity and the expiratory flow rate were calculated. The average of the best three and the best result were recorded for both the vital capacity and the expiratory flow rate. The volumes were corrected to standard temperature and pressure.

Sickness Absence.—The names of employees certified sick by their own doctors were sent via the labour departments to the health visitors. The health visitors' records were used whenever possible in order to obtain a precise diagnosis; when not available the labour department records were used. In this way all employees'

TABLE 8

AGE AND DURATION OF EXPOSURE OF THE EMPLOYEES IN THE THREE GROUPS IN 1954

Exposure (Years)	No Dust					Lime					Soda Ash				
	Age Groups					Age Groups					Age Groups				
	20–	30–	40–	50–	60–	20–	30–	40–	50–	60–	20–	30–	40–	50–	60–
6–	40	31	36	20	3	11	49	28	11	1	40	71	38	13	1
11–	—	—	12	25	8	—	1	7	7	1	6	6	14	12	2
21–	—	—	—	2	5	—	—	2	7	2	—	1	9	15	4
31–	—	—	1	3	—	—	—	—	2	3	—	—	1	5	2
41–	—	—	—	1	1	—	—	—	1	1	—	—	—	1	2

TABLE 9

AGE AND DURATION OF EXPOSURE OF THE EMPLOYEES IN THE THREE GROUPS IN 1956

Exposure (Years)	No Dust					Lime					Soda Ash				
	Age Groups					Age Groups					Age Groups				
	20–	30–	40–	50–	60–	20–	30–	40–	50–	60–	20–	30–	40–	50–	60–
6–	23	29	22	24	—	3	31	30	6	2	17	73	33	15	4
11–	1	—	2	11	2	—	—	5	10	2	2	17	16	10	3
21–	—	—	2	3	4	—	—	1	7	4	—	1	6	16	5
31–	—	—	—	1	2	—	—	—	1	4	—	—	1	6	—
41–	—	—	—	—	—	—	—	—	—	2	—	—	—	1	3

health records were obtained. The diagnoses were coded in accordance with the International Statistical Classification of Diseases. Hughes (1952) used this classification to indicate subgroups and two of his subgroups (upper and lower respiratory illness) were used for differentiation. Thus, the number of attacks and total weeks lost for each employee were ascertained.

Results

Industrial Dust Conditions.—The duration of exposure of the three exposure groups is shown in Tables 8 and 9. The concentrations of dust were determined by collecting the dust from a measured volume of air on a filter paper. The gradings of the dusts were measured by microscope counts on samples collected, on an electrostatic precipitator (Table 10). Representative points for dust collection were chosen. Most of the workers were placed in constant concentrations of lime dust and a central point was therefore chosen. Ash workers may be exposed to high or low concentrations depending on their work, and therefore both figures were noted. The advantageous effect of a good exhaust system is shown by the figures which do not indicate a high percentage of small particles.

TABLE 10

REPRESENTATIVE DUST PARTICLE CONCENTRATIONS IN COMPARABLE WORKING PLACES

Works		Average Dust Concentration $\left(\frac{mg.}{m^3}\right)$	Number of Particles Less than 4·5 μ per cu. ft./air	Particles Less than 4·5 μ (% by weight)
Lime:	A	8·82*	2,780	0·018
	C	2·1	662	
Soda Ash:	B	184·5 max.* 4·9 min.	745,000 19,800	0·215
	C	50·3 max. 2·1 min.	203,000 8,500	
No Dust:	D	0·3	89	0·017

* The concentration was much reduced later by dust extraction equipment already present at works C.

Sickness Absence.—Table 11 shows the sickness experience in contrasted dust exposure groups.

There were no significant differences between exposure groups in the mean frequency and time

TABLE 11

MEAN FREQUENCY AND TIME LOSS IN 1954

	No Dust Group			Lime			Soda Ash		
	Total No. in Groups	Attacks per Man	Weeks Lost/Man	Total No. in Groups	Attacks per Man	Weeks Lost/Man	Total No. in Groups	Attacks per Man	Weeks Lost/Man
Upper respiratory illness	188	0·505	1·65	134	0·619	1·552	243	0·531	1·38
Lower respiratory illness	188	0·181	0·856	134	0·164	0·604	243	0·152	0·514

TABLE 12

MEAN FREQUENCY AND TIME LOSS IN 1954 (95% CONFIDENCE LIMITS)

Between Groups	Weeks Lost per Man			Attacks per Man		
	Upper Respiratory	Lower Respiratory	Significance	Upper Respiratory	Lower Respiratory	Significance
No dust and lime	−0·83 to 1·78	−1·06 to 1·73	NS	−0·34 to 0·41	−0·25 to 0·26	NS
No dust and soda ash	−0·91 to 1·72	−0·99 to 1·85	NS	−0·31 to 0·36	−0·22 to 0·31	NS

NS = not statistically significant

TABLE 13

MEAN FREQUENCY AND TIME LOSS IN 1956

	No Dust Group			Lime			Soda Ash		
	Total No. in Groups	Attacks per Man	Weeks Lost/Man	Total No. in Groups	Attacks per Man	Weeks Lost/Man	Total No. in Groups	Attacks per Man	Weeks Lost/Man
Upper respiratory illness	126	0·508	1·56	108	0·805	2·20	229	0·611	1·39
Lower respiratory illness	126	0·182	0·849	108	0·296	1·41	229	0·170	0·620

TABLE 14

MEAN FREQUENCY AND TIME LOSS IN 1956 (95% CONFIDENCE LIMITS)

Between Groups	Weeks Lost per Man			Attacks per Man		
	Upper Respiratory	Lower Respiratory	Significance	Upper Respiratory	Lower Respiratory	Significance
No dust and lime	−0·85 to 1·99	−0·87 to 2·08	NS	−0·12 to 0·53	−0·14 to 0·36	NS
No dust and soda ash	1·10 to 1·20	−1·16 to 1·62	NS	−0·18 to 0·46	−0·18 to 0·26	NS

NS = not statistically significant

lost because of respiratory sickness absence (Table 12).

Two years later the same exposure groups' sickness absence (Table 13) showed that there was still no significant difference between the groups (Table 14).

In both instances a detailed study of the age-specific attack rates showed no important divergence between dusty and non-dusty groups.

Results of Chest Radiography.—Chest radiographs of 20 workers with long service and exposure to dust showed no abnormality and no evidence of pneumoconiosis on miniature films.

Physiological Tests

Vital Capacity in 1954.—In 1954 the statistical analyses related vital capacity to age in years, height in inches, and weight in pounds, for the three exposure groups.

TABLE 15

CHARACTERISTICS OF GROUPS AND MEAN VITAL CAPACITY IN 1954

Exposure Groups	No. Examined	Age (yr.)	Height (in.)	Weight (lb.)	V.C. (litres)
No dust	188	43·89	68·02	155·2	3·96
Lime	134	43·46	67·99	149·5	3·93
Soda ash	243	41·19	68·17	150·5	4·01

The regression coefficients (b) in the equation, $V = b_1A + b_2H + b_3W + \text{constant}$ are shown in Table 16.

TABLE 16

REGRESSION COEFFICIENTS

Exposure Groups	b_1	b_2	b_3
No dust	−0·0442	0·119	−0·00188
Lime	−0·0392	0·111	−0·00117
Soda ash	−0·0455	0·127	−0·00073

The regression coefficients for any group did not differ significantly from those of any other group, and they were, therefore, combined to give an overall estimate of the regression relationship, *viz*:—

$$V = -0{\cdot}0420A + 0{\cdot}132H + \text{constant}$$

The weight term is omitted since no coefficient differed significantly from zero.

The figures were further examined to see if a difference in vital capacity would appear in older men between the ages of 50 and 60. The results from 17 men from each group are shown in Table 17.

TABLE 17

CHARACTERISTICS OF GROUPS (OLDER MEN) AND MEAN VITAL CAPACITY

Exposure Groups	Age (yr.)	Height (in.)	Vital Capacity (litres)
No dust	53·6	68·0	3·33
Lime	54·1	67·53	3·61
Soda ash	54·0	67·65	3·32

The t test again showed that the most extreme difference, *i.e.*, that between the soda ash and lime areas, is not significant. It can, therefore, be concluded that there is no evidence that the vital capacity of men in these groups is affected by their environment.

Expiratory Flow Rate, 1954.—A regression analysis was done for expiratory flow rate similar to the analysis studying the dependence of vital capacity on age, height, and weight. The groups were the same. The regression coefficients (b) in the equation $M = b_1A + b_2H + b_3W + \text{constant}$ are shown in Table 18.

TABLE 18

REGRESSION COEFFICIENTS

Exposure Groups	b_1	b_2	b_3
No dust	1·25	2·38	0·20
Lime	1·34	2·52	0·09
Soda ash	1·23	1·63	0·11

As before, weight did not appear to be a factor affecting E.F.R. nor did the regression coefficients differ significantly between groups either for age or height. The overall relationship was:

$$M = -1{\cdot}19A + 2{\cdot}34H + \text{constant}$$

The average figures are shown in Table 19.

TABLE 19

CHARACTERISTICS OF GROUPS AND MEAN EXPIRATORY FLOW RATE IN 1954

Exposure Groups	No. Examined	Age (yr.)	Height (in.)	Weight (lb.)	E.F.R. (litres/min.)
No dust	188	43·89	68·02	155·2	104·06
Lime	134	43·46	67·99	149·5	97·44
Soda ash	243	41·19	68·17	150·5	98·23

If the expiratory flow rates are adjusted for age 42 years and height 68 in., common to all groups, they become:—No dust, 106·4; lime, 99·4; soda ash, 96·9.

The application of t tests showed that the differences between soda ash and lime groups and the no-dust group were highly significant (1·0%). This result was considered in relation to the radiographic and sickness-absence records of the exposure groups; it was felt that it should be confirmed in view of the negative findings in these two aspects of evidence of respiratory disability.

Thus, during the following year preparations were made to repeat the E.F.R. test on sample groups of 50 men from each of two works (B and C) and the control works D, drawn strictly at random from those tested in 1954. All aspects of the test, except the weight and height recording, but including the scene and time of year, were the same as in 1954.

The 1955 results (Table 20) were consistent with the linear regression relationship between E.F.R., age and height (M, A, and H) obtained in 1954.

TABLE 20

COMPARISON OF MEAN E.F.R. (1954-55)

Exposure Groups (50 in each)	Average E.F.R. (litres/min.)		Increase (litres/min.)
	1954	1955	
No dust	103·6	105·8	2·2
Soda ash: works C	103·3	115·0	11·7
Soda ash: works B	94·04	101·0	7·0

The marked increase in the E.F.R. in both groups exposed to soda ash compared with the non-dust group nullified any statistical difference found in 1954. This result was also remarkable as a slight fall in the E.F.R. should theoretically have been expected in all groups because of increase in age. It was, therefore, imperative to repeat the entire test in 1956 in order to confirm the 1955 findings. Thus, at the same time of year (July) and at the same site, the E.F.R. test was performed in exactly the same way as before. The 1954 volunteers were encouraged to repeat the test. The numbers obtained are shown in Table 21, together with the average E.F.R.

TABLE 21

COMPARISON OF MEAN E.F.R. (1954-56)

Exposure Groups	1954		1956	
	No. in Group	Average E.F.R. (l./min.)	No. in Group	Average E.F.R. (l./min.)
No dust	188	104·06	89	106
Lime	134	97·44	83	100
Soda ash	243	98·23	167	104

The results were on the average higher than those for 1954. For the means of these the average increase was 4·50 litres/min. (95% confidence limits, 3·22 to 5·78), which suggests that there are no systematic differences between the groups. This conclusion was confirmed by an analysis of variance in which the variation in the group average for 1956 was compared with the variation within the groups. The variation between group averages was not significantly greater than would have been expected if the groups had been identical.

Smoking Habits and Sickness Absence due to Respiratory Illness.—Oswald and Medvei (1955) in their investigation of London civil servants indicated the importance of smoking in respiratory disorders, particularly bronchitis. This has been confirmed by Doll and Bradford Hill (1956).

TABLE 22

MEAN CIGARETTES PER DAY OF EXPOSURE GROUPS IN 1956

Exposure Group	Number in Group	Cigarettes per Day
No dust	126	12·7
Lime	108	12·3
Soda ash	229	13·1

A comparison of the smoking habits of the three occupational groups in 1956 showed no difference (Table 22). The respiratory sickness absence attack rate for the three groups provides an indication of the effect of smoking (Table 23), based on one year's experience.

TABLE 23

SMOKING RELATED TO TOTAL RESPIRATORY SICKNESS (UPPER AND LOWER RESPIRATORY ILLNESS) ABSENCE IN 1956 (ATTACK RATE)

Exposure Group	Attacks per Man		
	0 to 5 Cigarettes per Day	6 to 20 Cigarettes per Day	Over 20 Cigarettes per Day
No dust	0·548	0·847	0.682
Lime	1·52	1·00	0·875
Soda ash	0·692	0·806	0·823

Table 24 shows the 95% confidence limits between the three smoking groups.

As there appeared to be a slight possibility of some significance in the no dust and lime groups, the analysis was repeated for the two groups 0 to 5 and over 21 cigarettes per day. The result is shown in Table 25.

There does not appear to be any significant difference in the total respiratory sickness absence between the three exposure groups attributable to smoking.

TABLE 25

95% CONFIDENCE LIMITS BETWEEN SMOKING AND TOTAL RESPIRATORY SICKNESS ABSENCES (MEAN FREQUENCY)

Exposure Group	Between 0 to 5 and over 21 Cigarettes per Day	Significance
No dust	−0·593 to +0·909	NS
Lime	−0·432 to +2·801	NS
Soda ash	−0·526 to +0·720	NS
All areas	−0·539 to +0·805	NS

S = statistically significant. NS = not statistically significant

Smoking Habits and Respiratory Tests.— A combined regression of expiratory flow rate on age and height (disregarding smoking) was worked out. This gave an average E.F.R. of 109·6 litres per minute; average age, 43·7 years; average height, 68·2 inches. The regression equation of E.F.R. (M) on age (X) and height (X_2) becomes:

$$M = -1{\cdot}27\,(X) + 3{\cdot}86(X_2) - 98{\cdot}1.$$

The 95% confidence limits for the two constants are:

$b = -1{\cdot}20$ to $-1{\cdot}35$. $c = +3{\cdot}44$ to $+4{\cdot}28$.

These slopes do not differ significantly from the 1955 random sample.

Tables 26 and 27 (Figs. 1 and 2) give the mean E.F.R. for the three smoking groups according to age and height.

Separate regressions were fitted to each smoking group.

The differences are significant, and indicate that moderate smoking (six to 20 cigarettes/day) increases the effect of both age and height. The effect of smoking in reducing E.F.R. is greatest for older and shorter men (Figs. 1 and 2). The group of men who smoke more than 20 cigarettes a day showed even steeper regressions, but as the number of men in the group was small and the results found were more variable than in the other groups, the differences in the regression constants are not statistically significant.

Discussion

Respiratory function tests have rarely been used on men exposed to alkaline dusts. However, Kadlec

TABLE 24

95% CONFIDENCE LIMITS BETWEEN SMOKING AND TOTAL RESPIRATORY SICKNESS ABSENCES (MEAN FREQUENCY)

Exposure Group	1956			
	Cigarettes per Day		Cigarettes per Day	
	Between 0 to 5 and 6 to 20	Significance	Between 6 to 20 and over 21	Significance
No dust	−0·07 to +1·09	Possible S	−0·53 to +1·23	NS
Lime	−1·01 to +2·16	NS	−0·09 to +1·31	Possible S
Soda ash	−0·18 to +0·92	NS	−0·028 to +1·22	NS
All areas	−0·26 to +0·27	NS	−0·14 to +1·05	NS

S = statistically significant NS = not statistically significant

TABLE 26

MEAN E.F.R. IN LITRES PER MINUTE BY AGE IN THREE SMOKING GROUPS

Age Group (Years)	0 to 5 Cigarettes per Day		6 to 20 Cigarettes per Day		Over 20 Cigarettes per Day	
	Number in Group	Mean E.F.R.	Number in Group	Mean E.F.R.	Number in Group	Mean E.F.R.
20–	11	118	33	122	2	117
30–	32	110	111	108	8	100
40–	32	102	68	98	18	98
50–	28	86	79	84	4	78
60–	12	80	21	71	4	56

TABLE 27

MEAN E.F.R. IN LITRES PER MINUTE BY HEIGHT IN THREE SMOKING GROUPS

Height (Inches)	0 to 5 Cigarettes per Day		6 to 20 Cigarettes per Day		Over 20 Cigarettes per Day	
	Number in Group	Mean E.F.R.	Number in Group	Mean E.F.R.	Number in Group	Mean E.F.R.
64–	28	97	50	89	6	63
66–	35	91	75	88	9	88·5
68–	31	108	112	101	9	92·5
70–	21	101	75	109	12	113

FIGS. 1 and 2.—The mean E.F.R. for the three smoking groups according to age and height.

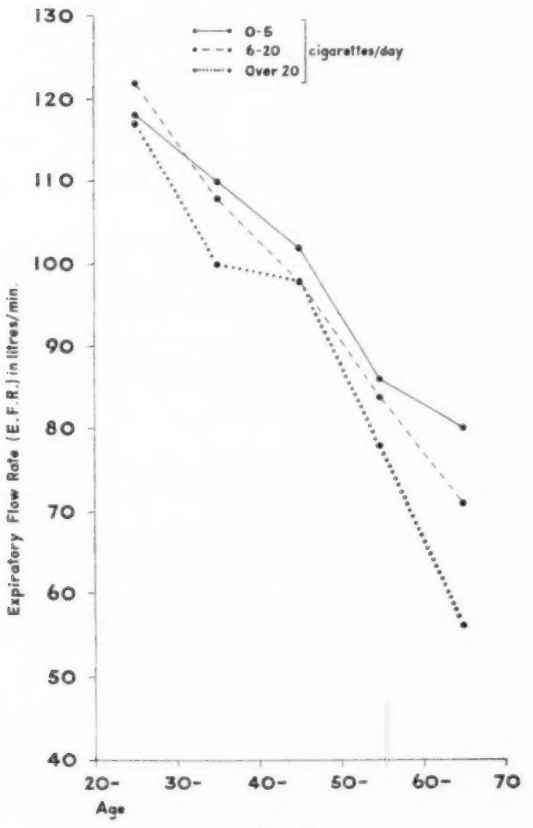

FIG. 1.

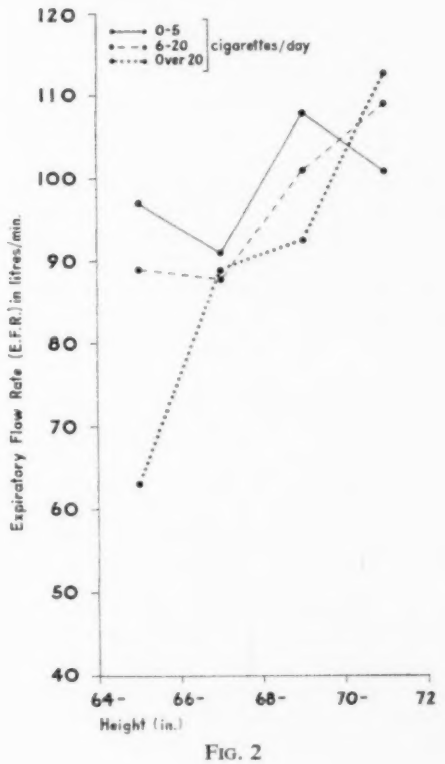

FIG. 2

and Vyskocil (1950) employed the fast expiratory vital capacity method for evaluation of the differences between three groups of workers in lime-containing cement. They had previously been graded by other functional tests and clinical and radiographic examinations into the three groups: slight bronchitis, advanced bronchitis, and doubtful emphysema. In 97 men who had been exposed to the dust for more than seven years, Kadlec and Vyskocil found statistically significant differences between the groups. Kazantzis and Buxton (1956) using the same test found no difference between control groups and groups exposed to cadmium fume. Gilson *et al.* (1955) considered that this type of test might be useful in assessing disability in pneumoconiosis particularly when compensation issues were at stake.

In the present paper the respiratory function of workers in alkaline dusts was compared with a control group using the expiratory flow rate test and, in contradistinction to Kadlec and Vyskocil's work, the affected groups were not previously subdivided according to respiratory disability. The findings in 1954 of a real difference in E.F.R. and no difference in vital capacity between the groups with a similar E.F.R. in the succeeding two years emphasized the importance of both the lack of morbidity and radiological evidence of effects from the dust. The E.F.R. test was chosen for its simplicity and had been used many times before the survey, but the stimulating effect of a group of men on each volunteer's efforts had not been appreciated. The uniform results obtained from the control group (works D) confirmed this view.

Sickness absence studies indicated that dust, particularly lime, does slightly increase the respiratory morbidity, a view which is in accord with that of Oswald and Medvei (1955).

Smoking habits coupled with respiratory morbidity and function tests indicated that heavy smoking combined with age and height in being significantly correlated with the E.F.R. This finding is similar to that of Whitfield, Melville Arnott, and Waterhouse (1951) who found a reduction in lung volume in heavy smokers. The older and shorter men had a greater impairment of the E.F.R. due to smoking. Respiratory sickness absence was also increased in heavy smokers. The implication from these findings was that, although the dusts concerned in the working environment do cause some increase in respiratory illness, their significance in the production of respiratory disability, either functional or pathological, is not as important as the number of cigarettes smoked daily.

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Brit. J. industr. Med., 1959, **16**, 61.

QUARRY BANK MILL

2. THE MEDICAL SERVICE

BY

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The first part of this essay was concerned with the development of the mill and with the social circumstances of the area at that time. This section deals with the nature of the medical service and the individuals responsible for it.

Medical Supervision

The first reference to the employment of a doctor was in 1789, and until 1795 the account books show that sums were paid on a number of occasions for medical attention to apprentices. The service began to be fully documented in 1804 and from then until 1847 there is preserved a continuous record of the visits of a number of physicians, some of whom are unknown, but of whom the most important were Peter Holland, Joseph Dean, and Joseph Nightingale.

Peter Holland (1766-1855) (Fig. 1).—Dr. Peter Holland, the son of a yeoman farmer at Sandlebridge near Knutsford, was apprenticed for three years at the age of 17 to Dr. Charles White of Manchester. (His deed of apprenticeship was seen by Brockbank (1904) though its present whereabouts are unknown.) After qualifying he went to practise in Knutsford, which was just outside the 10 miles radius of Manchester required by the terms of the agreement he had signed with Dr. White. Either he forgot his agreement or thought it a dead letter, for he was considered to be guilty of " poaching ", and in consequence he received in 1809 a lawyer's letter from White demanding the forfeit of £1,000. The matter was settled on " terms not stated ", said to have been by the intervention of the Earl of Stamford and Warrington, whose wife Holland had attended at Dunham Hall. He became a successful practitioner and very much respected in the county (Brockbank, 1904).

He married first, Mary, the daughter of the Rev. William Willets of Newcastle-under-Lyme and niece of Josiah Wedgwood, and had two sons and five daughters. His second wife was Mary Whittaker, daughter of Jeremiah Whittaker of Manchester, by whom he had two sons and one daughter (Burke's Peerage, 1953).

FIG. 1.—Peter Holland. (*By courtesy of Lady Malise Graham.*)

Charles Darwin, a grandson of Josiah Wedgwood, was his second cousin, and one of his sisters was the mother of Mrs. Gaskell, whose posthumous novel " Wives and Daughters " published in 1866 portrays a doctor, Mr. Gibson, who may well be a character study of her uncle. Stripped of the more romantic trappings of the novel (the ladies declared that he was " the illegitimate son of a Scots duke by a Frenchwoman "), he emerges as a tall, grave, rather handsome man with black hair and a sallow complexion, not at all jovial and with a rather

thistly dignity. He is sparing of his words, intelligent, slightly sarcastic, and " perfectly presentable ". He sends contributions to the scientific journals, studies botany as a hobby, and when Sir Astley (Cooper) comes to spend some time in the county he goes regularly to dine with him. He employs a succession of apprentices, two at a time, who lodge with him and, in the words of one character in the novel, " occupy an ' amphibious ' position " between the devil of medical education and the deep sea of romance with their master's daughter.

His son Henry (1788-1873) studied at Guy's and St. Thomas's and received the M.D. degree at Edinburgh in 1811. He was a most successful and fashionable London practitioner and a great traveller, visiting Iceland and contributing to Sir George S. Mackenzie's account of that island in 1810. He was medical attendant to the Princess of Wales (Caroline) on her continental visit of 1814 and later gave evidence in her favour during the scandal of 1820. He was made a Fellow of the Royal Society in 1816 and a Fellow of the Royal College of Physicians in 1828. Appointed physician-in-ordinary to Prince Albert in 1840 and to Queen Victoria in 1852, he was created baronet in 1853. He published an account of his travels in 1815, " Chapters on Mental Physiology " in 1852, " Essays " in 1862, and " Recollections of Past Life " in 1872 (Concise Dictionary of National Biography, 1948). His son, in turn, became the first Viscount Knutsford, and the present (4th) Viscount is therefore the great-great-great-grandson of Peter Holland.

Joseph Edward Dean (Died 1855).— The name of Joseph Edward Dean appeared in the main list of the Medical Directory for 1847 as of Wilmslow, Cheshire, but in 1848 and 1849 it was transferred to the supplemental list (of gentlemen who had not forwarded particulars of their professional qualifications and were therefore excluded from the main body of the Directory). In 1850 and 1851 this list was dropped and his name reappeared in the main list, but in 1852 the supplemental list was restored and his name remained in it, apparently unqualified, from then until 1855 (Royal College of Physicians, 1955; Guildhall Library, 1955).

Though there are no records of his medical qualifications, there are references to him in histories of Wilmslow. His house, of white stucco, stood in Bank Square on a site now occupied by a garden and a public lavatory. A water colour of 1899 looking up Church Street from the old village pump shows it quite clearly. In the year 1830 he was, in addition to being a busy practitioner, the village postmaster. At this time some 10 letters a day came to the parish. " Fortunately he had a large family and this enabled him to cope successfully with the delivery of letters to the various points of the district which lay so far apart " (Pearson, 1897). Another author gives no credit to the family:

> " One might suppose that the demands upon the time of a country practitioner whose duties called him at all hours to traverse a wide and thinly-peopled district would be ample, but Dr. Dean was like the Newcastle apothecary:
>
> ' Of occupation this was *quantum suff*,
> But still he thought the list not long enough,'
>
> and although there was no organized delivery, the 10 letters *per diem* which literally passed through his hands enjoyed a reasonable chance of ultimate delivery, for sooner or later the capacious pocket which contained a case of lancets in contact with a thin bundle of letters would appear at every corner of the parish " (Fryer, 1886).

The volume of letters increasing with the introduction of the penny post in 1840, Dr. Dean was obliged to give up his appointment as postmaster.

Joseph Nightingale (1796-1859?) L.S.A.—Only one document in the records of the Society of Apothecaries relates to Joseph Nightingale, namely, his qualifications. Its text is as follows:

" *Apothecaries Hall* 1796
Baptized
May 5, 1825 19 July
34. Mr. Joseph Nightingale, of full age, candidate for a certificate to practise as an Apothecary in (left blank), An Apprentice to Mr. Richard Nightingale, of Prestbury, Cheshire, Apothecary, for seven years. Indenture dated 23 April, 1816
Testimonial of moral Character: John Davis, M.D., Macclesfield
Lectures
2 courses on Anatomy and Physiology: Grainger
2 „ „ Theory and Practice of Medicine: Armstrong
1 „ „ Chemistry: Phillips
1 „ „ Materia Medica
Hospital Attendance
6 months at St. Thomas Hospital as P.P. (probationer physician)
Examined by Mr. Fallowfield and approved"

The date of his death cannot be ascertained from the Apothecaries' records, as he was never a member of the Society. The last time he appears in the Medical Directory is 1859, where the date of his qualification as L.S.A. is wrongly given as 1845. From 1851 onwards the entries under his name are asterisked, indicating that he had failed to make a return to the publishers of the Directory. Until 1847 he appears to have practised at Prestbury and thereafter at Wilmslow (Guildhall Library, 1955).

When the appointment of certifying surgeons became obligatory in 1844, Joseph Nightingale was appointed for the area including Quarry Bank Mill, and the registers containing his certificates of fitness of children and young persons for employment are still preserved there (Quarry Bank MSS).

Care of Apprentices

In a letter to the Rev. J. Sewell, who had written to enquire about the employment of apprentices, Samuel Greg replied that " the terms on which we take them are . . . (that) we keep them one month upon trial before (being) bound . . . to ascertain their probable healthiness ". If this appears to be a somewhat severe basis for a health service, it must be remembered that even nowadays there is seldom the grace of a month's probation and that in those days such a provision was revolutionary. Employers had to be on their guard, for parish authorities were anxious to be rid of children who were not physically fit, to the extent that " certain Poor Law officials stipulated that with every batch of children sent, a proportion had to be of this undesirable, *i.e.*, ' low I.Q.' type " (Lazenby, 1940). Some were only sent to factories when they had been misfits elsewhere.

In practice the service was not conducted on such rigid lines. There are numerous examples of children being kept for a year or more to see if their health improved. For example, the notes for February 28, 1833, contain the following:

> " Sarah Powell, Liverpool, aged 9. Healthy now. Had inflamed eyes a year ago but they are well now and there does not seem any objection to engaging her.
> *" Clara Harrison, Liverpool, aged 10. Has enlarged glands in the neck. Had better not be engaged at present.
> *" Mary Anne Hackett. Unhealthy. Must not be engaged.
> *" Sarah Macready. Aged 10. Eyes subject to inflammation. Not healthy.
> So much doubt about the three marked * that they had better not be engaged."

Clara Harrison and Sarah Macready, one month after, were both noted as " much more healthy than when she came " and their indentures were signed a year later.

Fanny Reece gave a great deal of trouble. She was first examined in December, 1833, aged 13, and labelled as " healthy, but seems weak in intellect—doubtful ". Nevertheless she was engaged, but after 1837 she appeared on almost every sick parade and seems to have spent most of her time being dosed with enemas, purgatives, emetics, or James's powders, and having rollers (bandages), splints, poultices, lotions, liniments, blisters, and leeches applied to sundry swellings of her neck and ankle.

Medical Records

The history of the medical services is contained in two cloth-bound foolscap notebooks which cover the period from 1804 to 1847. The first reference to a surgeon and apothecary is a note in the account books of the mill for a payment of £10 per annum in 1789. It is not clear if this sum was paid to Peter Holland, but it is certain that by 1795, in addition to being the Gregs' family doctor, he was looking after the apprentices for an annual fee of 12 guineas.

No medical records have survived for the period before 1804, but from that time until 1847 they appear to be complete. At first Peter Holland's hand-writing predominates, but in the second of the two books, begun in 1827, a cramped hand, believed to be that of Joseph Dean, becomes more frequent. Later, about 1840, the hand-writing of Joseph Nightingale makes its appearance. Occasional signatures of Peter Holland make it possible to distinguish between his hand-writing and Joseph Nightingale's, numerous signatures of Nightingale in the Register revealing a hand not greatly dissimilar. Entries, either by Dr. Holland's apprentices or other doctors from Wilmslow, occasionally appear, but most of the visits were paid by Peter Holland.

An interesting aspect of the records in the first of the two works is the combination of shorthand and longhand employed. Fig. 2 shows a page from the year 1805 in Peter Holland's hand. The shorthand represents the diagnosis or a clinical note, while the instructions to Mrs. Greg, who usually administered the treatment, are in longhand. It is interesting to find such a high standard of professional secrecy.

For a long time the deciphering of the shorthand presented apparently insuperable difficulties, but a chance encounter led to an introduction to Mr. William Carlton, an expert on early forms of shorthand. He recognized the method as one invented by Jeremiah Rich in 1646 and modified by a number of persons, among them Dr. Philip Doddridge, whose version, published in 1799, most closely resembles the system employed (Carlton, 1957).

The notes provide a fascinating insight into the limitations of the pharmacopoeia, the nature of medical practice at the time, and its application to industry. Visits were paid roughly at weekly intervals during the winter and every month during the summer, though numerous variations occur from year to year. In 1829, for example, only 14 apprentices were seen in a total of eight visits for the whole year, while in 1837, 68 visits were paid and 259 apprentices examined. The number of apprentices seen at each visit varied from one to a dozen, and groups of 20 to 30 were vaccinated at one time. Critics who maintain, with some truth, that this was mainly a treatment service on an *ad hoc* basis should remember that it was operating 150 years ago and that many so-called industrial medical services at the present time are not organized on such generous lines.

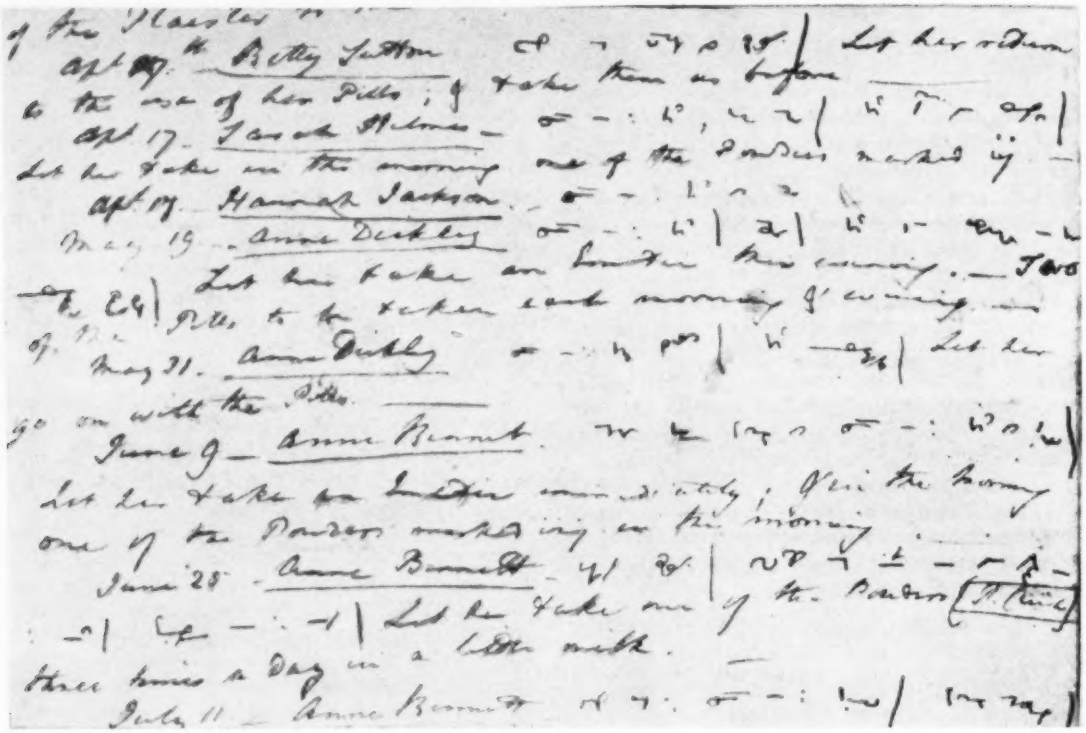

FIG. 2.—Facsimile of the case notes.

Apl. 17th *Betty Sutton* Complains of languor and debility. Let her return to the use of her Pills; and take them as before.
Apl. 17 *Sarah Helmes* Pain in the head, with fever. Has taken an emetic. Let her take in the morning one of the Powders marked iij.
Apl. 17 *Hannah Jackson* Pain in the head and fever.
May 19 *Anne Dickley* Pain in the head. Fever. Has been irregular in her menstrual discharge. Let her take an Emetic this evening. Two of the Pills to be taken each morning & evening.
May 31 *Anne Dickley* Pain in the head relieved. Has menstruated. Let her go on with the Pills.
June 9 *Anne Bennet* Fever with sickness and pain in the head and bowels. Let her take an Emetic immediately; & in the morning one of the Powders marked iij in the morning.
June 25 *Anne Bennett* Great debility. Cleared of matter in an abscess in the neck. Symptoms in the night. Let her take one of the Powders (P. Cinch.) three times a day in a little milk.
July 11 *Anne Bennett* Complains of the pain in the bowels. Sickness frequent.

Pre-Employment Examinations

Details are available of 292 pre-employment examinations. These do not include the apprentices employed before 1811 or after 1842, and cannot be a full list as 1,700 apprentices were employed between 1784 and 1847. There is some evidence of records having been kept on separate scraps of paper and of apprentices being sent after examination by an outside doctor. Out of these examinations, however, 203 were found healthy, 32 were said to be delicate, 28 had inflammation of the eyes, seven had enlarged glands, four were scrofulous, four were under age, one of whom was 6 years old, three had old injuries to arms, fingers or legs, one had scurvy, one was a bedwetter, one was weak in intellect, one was dwarfish, one had a discharging ear, one had weak ankles, one was " unhealthy ", and four were feverish at the time of examination (one scarlet fever).

Tuberculosis seems to have been common around the ages of 9 and 10, the average age at entry. Scrofula is probably tuberculous adenitis, enlarged glands usually refer to glands in the neck and under the jaw, probably of tuberculous origin, and the term " delicate " no doubt also includes tubercle.

Inflammation of the eyes affecting 10% of those examined may have been phlyctenular conjunctivitis, as there are references to it having left a " pearl ".

Its cause is unknown, though tuberculous infection is again a likely possibility. During the winter it must have been aggravated by the inadequate lighting and the smoke from tallow candles, until the installation of gas lighting in 1810. Small wonder that candle festivals celebrated the end of artificial lighting as the summer months approached.

Out of this group of 292 apprentices it appears that, apart from those under age, only five were not engaged. One had " opacities of both corneas—scrofulous appearance generally ", one had " gathering in the groin and cough ", another " too delicate and has a cough of long continuance but without pain in the chest ", yet another " weak eyes—subject to inflammation in them—does not appear to be stout ", and finally " unhealthy, must not be engaged ".

Mr. Samuel Henshall, the present manager of the mill, has undertaken the task of following up the history of each individual apprentice, and the more extensive details which emerge from this survey will be of the greatest interest.

The following are some typical entries from the pre-employment examinations, indicating the nature of the examinations and the attitude of the physicians:

Oct. 26, 1811.
Margaret Coppendale, aged 13, Newcastle. Subject to inflammation in the eyes. She is now free from this but it is to be feared that this may return on any exposure to cold. Her general habit does not appear strong.
Sept. 15, 1821.
Sara Wilson, aged 11, Burslem. Not a very strong girl, but appears free from complaints at the present time. Had better not be engaged until some trial has been given her.
(March 6, 1822.
Is quite well and her constitution seems improved.—P. Holland.)
Dec. 31, 1821.
Jane Wilson, aged 9, Liverpool. Has had inflammation in her eyes, which has left a Pearl. The inflammation will be very subject to return.
John Whitehead, aged 14, Liverpool. Has a small pearl on one eye, and it appears doubtful whether he is not subject to inflammation in the eyes.
April 23, 1820.
Anne Turner, aged 10, Newcastle. Has formerly had a fracture of the Elbow Joint, and cannot perfectly extend the arm. In other respects she appears healthy.
May 3, 1831.
Catherine Hupey, aged 9, Liverpool. Delicate: disposed to inflammation: a little cough. Had better not be hired.
(This has been scored out.)
Aug. 29: her eyes have remained well.
January 25, 1841.
Sarah Potts, aged 12¼. Slight appearance of scurvy. In other respects healthy.

In December of the same year Sarah makes her only appearance on sick parade when she is ordered brimstone and treacle every morning and ointment to her eyelids.

The last pre-employment examination was that of Elizabeth Bracegirdle on March 19, 1841. The note says "inflamed eyes. Not healthy". Her subsequent history is as follows:

Nov. 23*rd*, 1841: Four leeches round the right eye and in three days a blister behind the right ear, to be repeated in five or six days. To use the eye lotion to her eyes and to take half a white powder every night for six nights.
Dec. 17: To bathe her eyes in the warm chamomile tea frequently and have laudanum dropped into them at bedtime.
Jan. 2*nd*, 1842: To have wine of opium instead of laudanum dropped to her eyes at night.
Jan. 3*rd*: To have three leeches applied to the right temple today and three to the left temple on Friday. To bathe her eyes frequently with the eye lotion.
Jan. 5th: To have a blister behind the right ear and to take half a white powder each night.
Jan. 21st: To go on as before.
June 10*th*: If Elizabeth Bracegirdle comes home from Ashley, to apply a blister behind her right ear, as soon as that heals one behind the left ear, and then again behind the right ear, repeating them for a month; to keep her head very cool and her bowels open.
June 22*nd*: To follow the directions given on the 10th.
July 15*th*: To follow the directions given on the 10th June.

She does not appear on sick parade again.

Medical Treatment

On the whole, the therapy is of a similar heroic character. Much of it consists of purgatives—senna, calomel, rhubarb and ginger, jalap, salts, and " white powder ". Clysters are given frequently, blisters and poultices are common. Coughs are treated with horehound, ipecacuanha wine, and " cough pills ". Buttermilk and " churn whey " are regular beverages for the sick though on occasion red wine, broth, and tea are prescribed.

Accidents appear to have been rare. One entry reads " Thomas Jackson (arm caught in the mill), let a bread and milk poultice be applied twice each day ". A week later, " let him have a tablespoonful of the mixture three times a day and go on with the poultice ". After another five days " let him use the ointment to his arm instead of the poultice ". Nine days afterwards " let a little caustic be applied every other morning: dry lint and the cloth plaister ". Finally, a week later " to go on as before ".

" Cough with fever and pain between the shoulders " was treated as follows: " let him take one of the anodyne antimonial pills every four or five hours and a teaspoonful of salts in half a pint of tepid water each morning. Let a small blister be applied to the chest. *Flannel waistcoat* ".

" Itch " was treated with sulphur inside and out.

Sick apprentices were kept away from the mill. For example, Betty Clark, who had a blister applied to her left side, had to " live on milk, buttermilk, puddings, and vegetables and take no animal food. She had better be kept from the mill at present ".

Every page of the books has something of interest, a problem of diagnosis, an outmoded form of therapy, how the child reacted or how the doctor felt, and the general impression is of a standard of personal care above the level portrayed in the literature of the times.

Mortality

Although one of Samuel Greg's first acts was to purchase grave space for the interment of his casualties, the health of the children from the available evidence appears to have been relatively good. In addition to Ure's statement of mortality rates during apprenticeship, mentioned in Part I of this essay, R. H. Greg, the second son of Samuel, writing in 1837, quotes the same rate of one in 150 and compares it with the mortality rate of one in 120 at Christ's Hospital. He goes on to say " During the last 20 years there have been 17 deaths, eight boys and nine girls. The number of children has always been between 80 and 90, the age from 10 to 21 or normally 19. Of these, seven girls died in decline, one in consequence of inflammation in her eyes, one of apoplexy, three boys of decline, one of water in head, one of inflammation in the chest, one smallpox, one St. Vitus' dance which he had before coming to the mill and which at last threw him into decline, one killed by accident, but at play, not in the mill ". (Quarry Bank MSS.)

The reasons for this good record are probably the pleasant and healthy surroundings, the care which the apprentices received from the members of the family and the visiting physicians, and the fact that they were to some extent a selected population from which the obviously unfit were discarded.

Certainly E. H. Greg, a grandson of Samuel, regretted the passing of the apprenticeship system.

> " As a charitable institution none could surpass it, but it was finally broken up from difficulties arising from the Factories Acts, 'short time committees' and morbid philanthropy, and especially an official dislike or jealousy of trade, particularly the cotton trade " (Quarry Bank MSS).

Medical Treatment of Adult Workers

No record is available of the treatment of adult workers, though it is known that a dispensary was established in the early years of the mill and some of the notes in the doctors' day books probably refer to adults. In 1817 a Sick Club was formed, financed by contributions from the workers' wages and augmented by grants from Samuel Greg. The rules of the original Sick Club are lost, but they were revised in 1840, and a copy can be seen at the mill. It was a condition of employment that all persons over 13 years of age should belong, except married women, who had a separate Female Society formed in 1827. Contributions were at the rate of half a farthing in each shilling of their wages per week, and a committee of stewards was appointed to visit the sick and pay the benefits due, amounting to half-wages for not more than 12 weeks in a year. After one week's absence a medical certificate had to be produced before any further sum was paid. Death benefits varied from £1 to £10 according to seniority of membership and weekly contribution. The Club was merged in the 1860s in the Ancient Order of Gardeners, " Sowers Lodge ".

No evidence exists of any undue incidence of disease, but a warning note is struck by Samuel Finney (1785), who says:

> " This business has already had a visible bad effect on their countenances, producing a pale, sallow complexion, and occasioned the premature death of several young people of tender constitutions. But these are not all the evils this business has introduced. In such numbers of people, men and women, assembled together in this employment, there must inevitably be some profligates amongst them. These corrupt the rest and a general debauchery succeeds which alone would emaciate and enervate the body. The pernicious quality of the small particles of the cotton flying off their work gets into their lungs by respiration and clogs and impedes their freedom of play, and the very attitude of leaning upon the breast and stomach in which they are obliged to place themselves to work their jennies must have a very bad effect upon their health. Confinement also in crowded chambers where they must breathe a putrid air loaded with the films of cotton must have dreadful consequences . . . But in my opinion the men had better stuck to their husbandry business and the women and children to their jersey wheels if beauty, health, strength, activity and good morals are of any account in the lower class of people . . . And what advantage is the country to have for these evils. The enrichment of a few worthless people, ale-house keepers and low vulgar clowns, the masters, whilst their workpeople, though they receive great wages, are still poorer through their debaucheries than they were before."

It is known that several cotton mills employed doctors; Robert Blincoe (see Part I) describes his treatment at the hands of one of them; but no records of their visits or treatment, except in isolated cases, have been preserved. There is little or no evidence of a preventive approach at Quarry Bank, such as that later to be demonstrated by Charles Turner Thackrah, but the existence of the service at all is noteworthy, and it is believed to be the earliest example of an industrial medical service in England.

I am again indebted to Mr. Samuel Henshall for his guidance and his unique knowledge of the history of

the mill, to Dr. Finney for permission to quote from Samuel Finney's manuscript, to Mr. William Carlton for transcribing the shorthand, to Dr. Donald Hunter for discovering the photograph of Peter Holland, to Lady Malise Graham for permission to reproduce it, and to the librarians of the Royal College of Physicians and the Guildhall Library for their assistance.

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MISCELLANEA

Outbreak of Fever in Cotton Mills at Radcliffe, 1784

INTRODUCED BY

A. MEIKLEJOHN

From the Department of Industrial Health, University of Glasgow

In the Mackenzie Lecture published in this issue I have endeavoured to indicate the importance of this outbreak at Radcliffe in the development of measures to promote the health of factory workers. As appears from the sameness of quotations, often distorted by paraphrasing, few authors of medical and social essays on the period have read the report by Dr. Thomas Percival and his colleagues in the original text. The reason, of course, is that copies are rare and not easily accessible. It is hoped that the following reprint and library sources may be of interest and assistance.

A representation of a very alarming nature having been made by Lord Grey de Wilton, and a great number of the most respectable inhabitants of the township and neighbourhood of Radcliffe, in this county, to the gentlemen to whom the following letter is directed, of a malignant fever, which was supposed to have originated in the cotton works there; they took the liberty of desiring Dr. Percival, and the other medical gentlemen of Manchester, would take upon themselves the trouble of making such inquiries as they should think necessary, in order to ascertain the causes to which it was owing, and the most proper methods to be used to prevent the further spreading of the contagion. Much to the credit of the physicians, they undertook the task with the greatest alacrity, went over to the infected place themselves, and the following report was the consequence:

To

SAMUEL CLOWES, jun.
THOMAS B. BAYLEY,
DORNING RASBOTHAM,
and
M. BENTLEY. } Esquires,

HIS MAJESTY'S JUSTICES Of the PEACE for the County Palatine of LANCASTER.

GENTLEMEN,

WE have taken into the most deliberate consideration your very humane and judicious requisition; and we shall now lay before you the result of our inquiries, concerning those interesting objects, which you have proposed to our investigation. We have fully satisfied ourselves, either from actual observation, or authentic testimony, that a low, putrid FEVER, of a contagious nature, has prevailed many months in the cotton mills, and among the poor, in the township of Radcliffe. We cannot, however, ascertain whether this fever originated in those works, or was imported into Radcliffe from some other parts of the county. But though this point remains doubtful, we are decided in our opinion, that the disorder has been supported, diffused, and aggravated, by the ready communication of contagion to numbers crowded together; by the accession to its virulence from putrid effluvia; and by the injury done to young persons through confinement and too-long-continued labour: to which several evils the cotton mills have given occasion.

These evils, we trust, are not without remedy; and from the benevolent attention which the proprietors of the Radcliffe works have shewn to the sick and infirm under their charge, we may reasonably presume to hope they will be induced to adopt the following practicable regulations, from motives of policy, humanity, and justice, as well as from the respect which is due to your authority:

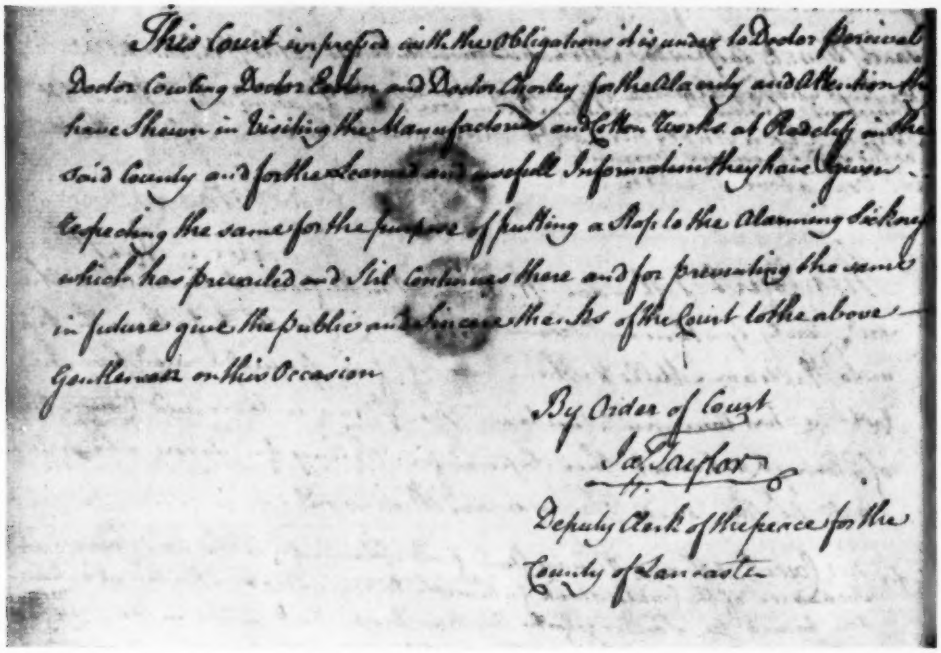
I. All the casements of the windows, and the three large western doors of the cotton mills, should be left open every night: the same regulation should take place during the recess from work at noon; and as many casements should be kept open in the hours of labour as may be compatible with carrying on the operations of the machinery.

II. The casements are too small, being in dimension only about one sixth part of the window: they are likewise placed high, and parallel to each other, a position obviously unfavourable to complete ventilation; for the inlet of the air ought to be lower than the outlet.

III. Several fire places, with open chimnies, should be erected, at proper distances, in each work room. The stoves now employed afford no sufficient passage for the offensive vapours generated in the rooms, and increase the contamination of the air by the effluvia which they emit. Turf would be the cheapest, and also a very salutary fuel; for it consists chiefly of the roots of vegetables, and yields, in burning, a strong, penetrating and pungent smoke, which is likely to prove as good an antidote to contagion as that of wood is found to be from long experience.

IV. The rooms should be daily swept, and the floors washed, at least once every week, with strong lime water, or with water impregnated with the spirit of vitriol or the acid of tar. The walls and ceilings may be scraped and whitewashed, at first, every month, and afterwards twice or thrice yearly. Lime, fresh burnt, and as soon as it is stacked, must be used for this purpose, and the wash laid on whilst it is hot.

V. During the prevalence of the present fever the apartments should be fumigated weekly with tobacco.



This Court impressed with the Obligations it is under to Doctor Percival Doctor Cowling Doctor Eason and Doctor Chorley for the Assiduity and Attention they have shewn in visiting the Manufactories and Cotton Works at Radcliff in the said County and for the learned and useful Information they have given respecting the same for the purpose of putting a Stop to the Alarming Sickness which has prevailed and still continues there and for preventing the same in future give the public an Entire Approbation of the Conduct of the Court to the above Gentlemen on this Occasion

By Order of Court
Jas Taylor
Deputy Clerk of the Peace for the
County of Lancaster

The original of this document dated October, 1784, is in the Lancashire County Record Office, by whose courtesy this reproduction is published.

Brimstone might, perhaps, be more powerful; but, in burning, it yields an acid which would be injurious to the cotton.

VI. Great attention ought to be paid to the privies: they should be washed daily, and ventilated in such a manner that the smell arising from them shall not be perceptible in the work rooms.

VII. The rancid oil which is employed in the machinery is a copious source of putrid effluvia. We apprehend that a purer oil would be much less unwholesome, and that the additional expense of it would be fully compensated by its superior power in diminishing friction.

VIII. A strict observance of cleanliness should be enjoined on all who work in the mills, as an efficacious means of preventing contagion, and of preserving health. It may also be adviseable to bathe children occasionally. The apparel of those who are infected with the present fever should be well fumigated before it is again worn; and the linen, etc., of the sick should first be washed in *cold* water, lest the steams arising from heat communicate the distemper to the persons engaged in that operation. Crofter's lye, when it can be procured, is preferable to water. The bodies of those who die of the fever should be closely wrapped in pitched cloth, and interred as soon as propriety or decency will permit. Smoking tobacco will be an useful preservative to the superintendents of the works, and to others exposed to infection who can practise it with convenience.

IX. We earnestly recommend a longer recess from labour at noon, and a more early dismission from it in the evening, to all those who work in the cotton mills: but we deem this indulgence essential to the present health, and future capacity for labour, of those who are under the age of fourteen; for the active recreations of childhood and youth are necessary to the growth, vigour, and the right conformation of the human body. And we cannot excuse ourselves, on the present occasion, from suggesting to you, who are the guardians of the public weal, this further very important consideration, that the rising generation should not be debarred from all opportunities of instruction at the only season of life in which they can be properly improved.

We have the honour to be, with the highest respect,
Gentlemen,
Your most faithful and obedient humble servants,
Thomas Percival, M.D.
John Cowling, M.D.
Alexander Eason, M.D.
Edward Chorley, M.D.

Manchester,
October 8th, 1784.

P.S. Our respectable colleagues, Dr. Mainwaring and Dr. Mitchell, are absent from Manchester at this time.

SOURCES

The reprint is from *Thoughts upon the Means of Preserving the Health of the Poor by prevention and suppression of Epidemic Fevers. Addressed by the inhabitants of the Town of Manchester and of the several Populous Trading Towns surrounding and connected with it*, by the Revd. Sir Wm. Clerke, Bart., London, MDCCXC. (from the Library of the University of Edinburgh, volume entitled Pamphlets on Infirmaries, number LL.116.5.24: pamphlet 22).

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Occupation and Mortality*

Filial Mortality

In an altogether too close and prolonged professional acquaintance with the Registrar General's Classification of Occupations one has often pondered the risk of being the son (or daughter) of men in different walks of life. It has, for instance, always seemed that there must be something chancy about the home background provided by a drowner (Code No. 029), ripper (044), bruiser (352), lynchman, scalper, gunman, first time mangler, or acid bath worker. What is the ultimate fate of the children of doublers, twisters, slickers, forgers, lurers-off, and vice folders? How delightful to be the child of a Christmas pudding worker, turkish delight maker, toffee dipper, or jelly boiler. And what happens when your father is a bogeyman or wizard?

These, and other similar questions provoked by this "Arabian Nights" collection of occupational descriptions might, one felt, have been answered by that part of the Registrar General's Decennial Supplement which deals with occupational mortality, and in particular with infant mortality. Any such hope was doomed to disappointment. These particular axes of classification have been unaccountably neglected. There is, nevertheless, a great deal of material in the section on infant mortality and stillbirths which is of interest to doctors in industry. For, though it may not be immediately apparent why the infant mortality of the children of men in different occupations should be a suitable subject for review in this *Journal*, a short examination of the data is enough to show how close is the relationship between the death rates of men in different occupations and the mortality of their babies. The mortality of their infants, moreover, together with the mortality of their wives (used for this purpose for the first time in the 1931 report), is a useful indicator of the healthiness of the men's home environment. It may thus help to determine whether a particular high mortality, which might appear to be a direct result of the men's calling, is or is not more likely to be attributable to the general factors which affect also their wives and children.

Social Class.—In this analysis of the mortality in the five years 1949-53 the well-known trend of infant mortality with social class appears, as it has in every previous analysis that has been made in the series of decennial supplements. This is in contrast to adult mortality where, for the first time, the analysis based on the data of the 1951 census shows an irregular trend with class. Nor is there any material decrease in the slope of the trend of infant mortality with social class compared with previous years. The differentials are much the same as they have always been in spite of the enormous reduction in the rate since say, 1921 (Fig. 1, c.f. Morris and Heady, 1955). Details of the social class trends are shown in Table I, where it will be seen that (again as usual) the class trend is much more pronounced in post-neonatal mortality (infant mortality after four weeks) than in neonatal mortality. The class trend in the stillbirth rate is also shown for the first time in this series of reports, and it will be seen that the gradient is similar to that of the neonatal mortality rate. Social class trends for some specific causes are also shown. The general picture is familiar to students of the subject, a striking gradient for pneumonia, gastro-enteritis, and deaths ascribed to "immaturity"—not so striking for congenital malformations. This is the first time in this series of supplements, however, that a class gradient in this direction for death due to birth injury has appeared.

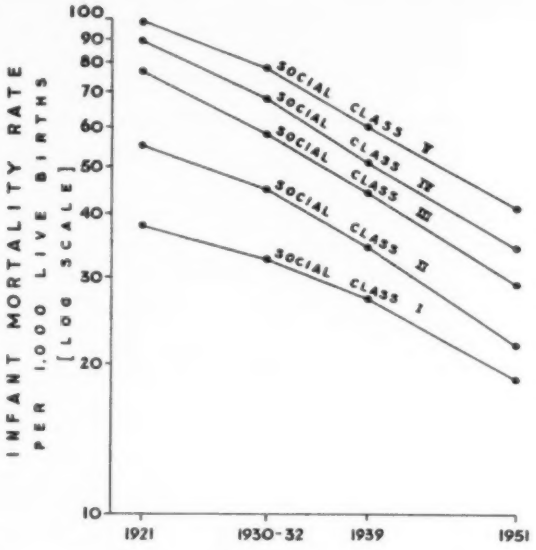

FIG. 1.—Decline in infant mortality in five social classes in England and Wales in 1921-51 for legitimate births.

Variations in infant mortality in different parts of the country are reported annually in the Registrar General's Statistical Review. The present volume shows that, broadly speaking, the social class variations in neonatal mortality, post-neonatal mortality, and the stillbirth rate described above were reproduced in each of the major regions of the country, and in rural as well as in urban areas. Conversely the regional pattern of high mortality in the north and west and low mortality in the south-east was broadly similar in each class.

Occupational Groups.—So far the results have been discussed in terms of social class, but of course each class is the aggregate of many different occupations, and the second volume of this report on occupational mortality gives the infant mortality and stillbirth rates of children of men in the 600 odd occupations which have a separate

*General Register Office (1957). *The Registrar General's Decennial Supplement, England and Wales (1951) Occupational Mortality*, Part II, vol. 1 and 2.

TABLE I

SOCIAL CLASS TRENDS IN INFANT MORTALITY
ENGLAND AND WALES, 1949-53. LEGITIMATE INFANTS

Social Class	Infant* Mortality	Neonatal* Mortality	Post-neonatal* Mortality	Stillbirth Rate†	Infant Mortality* from Five Selected Causes				
					Pneumonia	Gastro-enteritis	"Immaturity"	Congenital Malformations	Birth Injury
I—Professional, etc.	18·7	14·0	4·7	16·3	1·9	0·5	3·9	3·6	2·1
II—Intermediate	21·6	15·6	6·0	19·9	2·7	0·7	4·6	3·6	2·4
III—Skilled workers	28·6	18·3	10·4	22·5	4·6	1·4	5·7	4·5	2·7
IV—Partly skilled workers	33·8	20·0	13·7	24·5	6·2	1·9	6·4	4·8	3·0
V—Unskilled workers	40·8	22·8	18·0	27·4	8·2	2·9	7·6	5·1	3·0
All classes	29·5	18·6	11·0	22·8	4·9	1·5	5·8	4·5	2·7

*Rate per 1,000 live births.
†Rate per 1,000 live and stillbirths.
Neonatal mortality, *i.e.*, deaths at ages under 4 weeks.
Post-neonatal mortality, *i.e.*, deaths at ages 4 weeks to 1 year.
For full details see Tables ES, EX, and FK of the commentary volume.

TABLE II

OCCUPATIONAL GROUPS WITH HIGHEST AND LOWEST INFANT MORTALITY RATES
ENGLAND AND WALES, 1949-53. LEGITIMATE INFANTS

Occupational Group No.	Description	Social Class	Infant Mortality	Stillbirth Rate
	A. *Ten Groups with Highest Rates*			
4	Coal-miners (coalface coal getters, loaders)	III	46·9	29·4
5	Coal-miners (workers below ground, not coalface)	IV	43·1	26·7
19	Iron foundry labourers	IV	42·4	25·0
10	Coal-miners ("other" workers, above ground)	IV	40·7	31·0
40	Openers, sorters, blenders, carders, etc. (textile)	III and IV	40·7	24·4
82	Costermongers, newspaper sellers, and other hawkers	V	39·9	27·6
69	Locomotive engine drivers and motormen	III	39·4	26·3
61	Platelayers	IV	38·9	32·0
58	Builders', bricklayers', plasterers', masons' labourers	V	38·3	25·8
18	Iron or steel foundry furnacemen	IV	38·1	*23·0*
	All occupations		29·5	22·8
	B. *Ten Groups with Lowest Rates*			
85	Clergymen (Church of England)	I	16·2	17·0
89	Registered medical practitioners, radiologists	I	16·7	13·2
66	Civil service and local authority administrative and executive officers	I and II	17·4	18·0
91	Teachers (not music)	II	17·7	17·0
92	Professional engineers, surveyors	I	17·7	16·5
87	Ministers of other religious bodies, *i.e.*, not C. of E. or R.C.	I	*17·8*	*19·0*
31	Radio and radar mechanics	III	17·8	17·0
88	Judges, barristers, etc., solicitors	I	19·3	12·9
76	Owners, etc., of wholesale businesses	II	19·7	18·0
93 and 94*	Armed forces, commissioned officers, (active and retired)	I	20·0	14·9

*These two occupational groups have been combined to form the tenth in this table since their infant mortality and stillbirth rates are not given separately.
Rates calculated on less than 50 deaths are shown in italics. None of the rates is calculated on less than 30 deaths.

code number in the Classification of Occupations (Registrar General, 1951). The first volume, which is the commentary on the tables in the second volume, does not deal with this information in any detail, presumably for reasons of space, and of course there is no room for extensive treatment here. Since, however, analysis of the social class variation in infant mortality in terms of the constituent occupations and groups of occupations can be revealing, it seemed worth while at least to compute the infant mortality and stillbirth rates of the 110 "occupational groups" which the Registrar General uses for detailed analysis of the adult mortality by age and cause of death. The 10 occupational groups with the highest infant mortality rates and the 10 with the lowest rates are shown in Table II, together with the corresponding stillbirth rates and the social classes to which the individual occupations which make up the groups are assigned. This table is interesting for the additional information it gives over and above the usual picture of infant mortality as being closely determined by "social class". The occupations in each of these extreme groups do not by any means come only from the social classes at either end of the class scale. Miners in Social Class III have the highest rates, while one occupation from Social Class III figures in the 10 groups with the lowest rates. High income is no essential qualification for inclusion amongst the group with the lowest rates. Clergymen, teachers, and civil servants are not the richest of the rich. Nor is very low income the hall-mark of the man in the high risk group. It is true, of course, that no occupations from social classes I and II appear amongst the 10 with the highest rates, nor do any from classes IV and V

TABLE III

INFANT MORTALITY, STILLBIRTHS, AND ADULT MALE MORTALITY IN OCCUPATIONAL GROUPS WITH HIGH AND LOW MORTALITY RATES. ENGLAND AND WALES, 1949-53

Occupational Group No.	Description	Infant* Mortality	Stillbirth* Rate	Male S.M.R., at Ages 20 to 64, for			
				Respiratory Tuberculosis	Chronic Rheumatic Heart Disease	Pneumonia	Bronchitis
10 Occupational Groups with Highest Infant Mortality Rates							
4	Coalface getters and loaders	159	129				
5	Coal-miners below ground	146	117	119	110	112	135
10	Coal-miners above ground	138	136				
19	Iron foundry labourers	144	110	130	*104*	212	177
40	Openers, sorters, blenders, carders, etc.	138	107	*54*	*135*	*127*	156
82	Costermongers, hawkers, etc.	135	121	167	*104*	173	178
69	Locomotive engine drivers and motormen	134	115	65	*68*	65	86
61	Platelayers	132	140	77	*59*	*94*	98
58	Building trade labourers	130	113	178	131	166	178
18	Iron and steel foundry furnacemen	129	*101*	(*82*)	(*25*)	(*120*)	*100*
10 Occupational Groups with Lowest Infant Mortality Rates							
85	Clergymen (C. of E.)	55	75	*40*	*87*	(*40*)	(*10*)
89	Registered medical practitioners	57	58	*49*	*48*	*59*	*24*
66	Civil Service and local authority administrative and executive officers	59	79	45	58	43	30
91	Teachers (not music)	60	75	29	57	*33*	21
92	Professional engineers, surveyors	60	72	42	*44*	*49*	28
87	Ministers of other religious bodies (not C. of E. or R.C.)	*60*	*83*	*40*	(*33*)	(*27*)	(*7*)
31	Radio and radar mechanics	60	75	*82*	*108*	(*30*)	(*38*)
88	Judges, barristers, etc., solicitors	65	57	*58*	*59*	*63*	*26*
76	Owners, etc., of wholesale businesses	67	79	47	65	63	49
93	Armed forces, officers—active	68	65	*32*	(*17*)	(*22*)	(*74*)
94	Armed forces, officers—retired			237	*91*	*80*	*77*

*Infant mortality and stillbirth rates are expressed as a percentage of the rate for all occupations for ease of comparison with the S.M.R.s. The rates are shown in Table II.

S.M.R.s calculated upon less than 50 deaths are shown in italics, those calculated on less than 10 deaths are also enclosed within brackets.

The S.M.R.s for the separate occupational groups in the coal-mining industry are not shown because of the doubt cast in the report itself on the validity of such distinctions.

appear amongst the 10 with the lowest rates. Apart, however, from this general agreement these occupational groups cut across most of the accepted social classifications, except perhaps the ancient social stratification of those who do the rough work and those who don't. For the 10 with the highest rates include several from really "black" industry—coal-miners, foundry labourers, furnacemen, plate-layers—almost brute labour so far as it now exists. At the other extreme are "white collar" jobs where no-one is likely to get his hands dirty. On the whole it will be seen that the stillbirth rates correspond with the infant mortality rates.

Comparison with Mortality of Adult Males.—Further interest is added to the infant mortality rates of the children of men in these occupations when the mortality of the men themselves is considered. Table III takes the same occupational groups and gives their standardized mortality ratios for four causes of death—respiratory tuberculosis, chronic rheumatic heart disease, pneumonia, and bronchitis—which, like infant mortality, show, and have shown since "social class" was invented, a striking class gradient, with high mortality in social class V. For each of these causes this class gradient is present also for the wives of men in these classes. They are therefore four thoroughly class-conscious killers. For ease of comparison the infant mortality and stillbirth rates have been dressed up to resemble standardized mortality ratios, *i.e.*, the rate has been expressed as a percentage of the rate for all classes or occupations. It will be seen that, with some exceptions which are themselves interesting, where the infant mortality rate is low the mortality from these four causes is also low, and where the infant mortality is high the mortality from these causes is high. This is, of course, partly a consequence of the fact that, in each case, the class trend is similar to the class trend for infant mortality. But this is not the whole story, for, as has been stressed above, the occupations do not follow the class pattern at all rigidly, though conforming to it in a general way. It is interesting that these four conditions, in three of which the mortality has declined, though for different reasons, while mortality in the fourth remains obstinately high, should show this degree of similarity in their occupational distribution, both amongst themselves and with infant mortality. It can be seen from this table also how useful, in a question-raising way, it can be to put side by side the occupational mortality for adult males, adult females, and their children. The high rates for pneumonia and bronchitis in foundry workers, for instance, is not so obviously and wholly occupational in origin when it is known that their infants also have a high mortality, especially since respiratory infections comprise nowadays the most important single group of causes of infant death. Conversely, the relatively low adult mortality from these four causes of engine drivers, motormen, and platelayers contrasts strangely with the high infant mortality of their children.

Individual Occupations.—The next, more detailed, stage in classification of occupational groups consists of those occupations designated by a single code number in the Classification of Occupations and reveals even higher infant mortality and stillbirth rates. Limiting the discussion to those occupations where there were 50 or more infant deaths (or stillbirths) in the five years one finds the infants of kitchen hands and of other indoor domestic servants with mortality rates of 55·3 and 61·0 per thousand respectively; of " other fitters " with a rate of 60·3; of fishermen with 55·1; of plasterers' labourers and drivers of horse-drawn vehicles with 50·1; and of non-ferrous foundry furnacemen with 50. Stillbirth rates in the 40s are also returned though the groups concerned are not very closely defined, being largely such categories as " other fitters " (with a rate of 47 per thousand), etc. There were no single occupations with rates appreciably lower than for the occupational groups shown in Table II B.

* * *

Clearly there is scope for much quarrying of this mine of material and much speculation on the reasons for such differences. Current theories about the importance of the quality of maternal care, of the mother's education, of the different customs of child care handed down from mother to daughter, of the mother's childhood background, of the differences in availability and of summoning medical help, of the spread of infection, can receive support and discouragement from these figures. There is no space to do more than indicate the extent of the information available.

Reliability of Occupational Data.—One further general point should be mentioned, namely the reliability of the occupational data. In dealing with adult mortality the Registrar General has, very honestly, raised important doubts about the validity of the rates he has published. This is largely because the information about occupations comes from two sources, from census schedules for the " population ", or denominator of the mortality rate, and from the death registration documents for the deaths, or numerator of the rate. These may not tally for various reasons: changes of job which mean that the distribution of jobs at the census does not reflect the distribution over the five-year period, differences between census description and death registration description of the same job (in the one case by the man himself and in the other by his widow, for instance) and so on. Moreover, the man may have changed his job because of the illness which finally kills him. Important as these effects may be in adult mortality they are likely to be less important in the analysis of infant mortality by the father's occupation. For, though information about the numerator and denominator comes from two sources as in adult mortality (in infant mortality the two sources are birth and death registration), the first volume of the present report on occupational mortality describes the results of a special enquiry which shows clearly that the effect of such differences is unimportant in infant mortality. In stillbirths, of course, they do not arise. It is also clear that the father will rarely change his job because his child is ill, so that another reason for doubting the validity of adult occupational mortality rates is not present in the statistics of infant mortality. One particular group of occupations, the validity of whose adult mortality rates has been most seriously questioned in the report, is the group concerned with coal-mining; particularly where comparisons are made between different occupations within the industry. In infant mortality, these difficulties are unimportant since the rates for all three groups of miners distinguished in Table IIA are similar and all well above average.

The fact that differences between the descriptions of occupations on two different occasions, and, quite likely, by two different people, do not appear to affect the validity of infant mortality rates to an important extent alleviates, though it by no means disposes of, corresponding doubts about adult occupational mortality rates. It also adds authority to the evidence mentioned above, on the parallelism of decline of infant mortality rates in different classes and occupational groups over the past few decades.

J. A. HEADY

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Mortality in Mining and Quarrying Occupations

Mining is a good example of the caution needed in the interpretation of death rates tabulated by occupation. The report of a standardized mortality ratio above the national average raises two questions: Is it correct, and, if correct, does it necessarily imply a hazard to life specific to the occupation? As the Registrar General points out in this section of his Commentary, studies designed to answer these questions have been sponsored by the National Coal Board and carried out, with the help of the Board and the General Register Office, in the Department of Medical Statistics and Epidemiology at the London School of Hygiene and Tropical Medicine. The first report of the work was recently published (Heasman, Liddell, and Reid, 1958). Briefly, a comparison of occupation as given either by the informant at the time of death registration or as ascertained by local inquiry largely at the pit where the dead man used to work showed quite serious discrepancies. In general, there was a marked tendency for " promotion " from retirement or doing another job back to the mine; and within the mine, men tended to be described by the informant as coal-face workers. Again, where the description was the rather vague one of " coal-miner ", the General Register Office coding conventions assigned the death to the faceworker category. To a lesser extent, the same trends operated even in self-description at the time of census. Although these similar errors in assignment tended to cancel each other out, the net result was still an inflation of the reported death ratio for miners in general and faceworkers in particular, it seemed likely, in fact, that miners do not have a death rate much above the national average and that among men whose

last occupation was at the coalface the death rate was substantially lower. The effect of selection in original choice of job and later selective elimination is thus obvious.

The limitations of the conventional mortality rate by last occupation as a measure of the specific occupational risk to life thus made plain are emphasized by the Registrar General who confines his discussion largely to the experience of coal-miners as a whole. He also relates present death rates in this occupational group to the history of the industry in the present century. The moribund state of coal-mining in this period was reflected in fewer young men joining the labour force and the drift away from the more depressed areas to other mines or to alternative jobs in other parts of the country. These movements within the industry as new coalfields expanded and others shut down caused low death rates in the new districts which have attracted the younger and fitter men and, conversely, high rates in the derelict areas with an older residual population. Outside the industry, the bringing of new alternative forms of employment to a mining area may also have drawn off the younger and fitter men. It is thus not surprising to find that, when accidents have been dropped from the account, miners' mortality is, relative to that of other men, worse at ages over 55; and the position has deteriorated since the last census.

Despite the admitted imperfections of these death rates by occupation, certain hazards to health are still clearly revealed. Accidents among the younger men and the dust diseases of the chest stand out above any likely artifact due to inadequate descriptions of jobs on death certificates or census schedule. As usual, the South Wales anthracite fields have the highest rates in this latter respect. On the other hand, the general tendency towards inflation of death rates underlines the significance of the death rates from lung cancer, vascular lesions of the central nervous system, and coronary thrombosis which, particularly among the underground workers, are well below the national level. Cancer of the stomach seems to be the only malignant disease which causes an excessive death rate among miners.

The death rates among miners' wives are doubtless subject to the same sort of bias in reporting of occupation as those of their husbands. To that extent, therefore, their value as a control of the component of social environment in mortality is limited. Nevertheless, the consistency of the pattern of death rates by cause in the two sexes does suggest that some of the excess mortality among miners, *e.g.*, from tuberculosis, bronchitis, or cancer of the stomach, may be socially rather than occupationally determined. But miners' wives also have disabilities not shared by their husbands: an excessive mortality from all causes even in early adult life and from all the cardiovascular-renal group of disorders at all ages. For suicide at least, both miners and their wives have a relatively low rate.

Some of the problems of interpretation encountered in the coal-mining industry exist for the death experience in other forms of mining in this country. Tin and copper mining, for example, is a dying craft subject to the selective loss of the younger and fitter men. Even for the period covered by this Occupational Supplement, however, it is difficult to explain 78 deaths from industrial pulmonary disease instead of the one expected except on the basis of a serious and specific occupational risk. For " getters in open quarries " some of these occupational hazards were serious enough, but in general their death rates differed little from the national average.

D. D. REID

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Mortality in Transport Occupations

Difficulties of interpretation, to which the Registrar General refers in his introduction, apply in full measure to the data for transport workers. First, the classification of the data may lead to misunderstanding. For example, the number of " railway transport workers " is about half the total employed by British Railways because engineering, clerical, and miscellaneous grades have been omitted. Only operating grades are covered, and the heading " railway officials " is similarly restricted. By contrast, bus and tramway managers are included among transport workers.

Secondly, mis-statements of occupation are probably frequent. For example, it appears that many owner-drivers of taxis, returned at the census as drivers, are included on death among car and coach hire proprietors; the standardized mortality ratio (S.M.R.) of this group is no less than 427.

Thirdly, public safety demands selection on entry and, subsequently, transfer of the unfit to less responsible posts. This makes it difficult to associate mortality with occupational factors.

This last difficulty is illustrated by the overall S.M.R.s for the various groups of railway workers. The groups with low S.M.R.s are engine drivers (93), firemen (86), guards (86), and signalmen (83). Average figures occur among railway officials (95), shunters (103), porters (104), and running shed workers (96). The only significantly high S.M.R. is for ticket collectors (135). Collecting tickets is not evidently detrimental to health but ticket collectors include many rejects from other grades.

The point is further illustrated by deaths from bronchitis which are higher than expected among ticket collectors, porters, and running shed workers (all receiving grades for chronic bronchitis), and lower among railway officials and signalmen. Deaths from tuberculosis also are higher than expected among ticket collectors and lower among officials, drivers, guards, and signalmen. Coronary diseases, the sudden onset of which may preclude transfer to other work, caused deaths above expected among officials and drivers, below expected among porters.

Deaths from accidents not in the home were above expected among drivers, firemen, guards, and shunters. Deaths from leukaemia were higher than expected for officials and drivers but not significantly different from the expected level for other railway workers. Signalmen enjoyed a low death rate for cancer.

For many groups of road transport workers inter-

pretation of the figures is made difficult by mis-statements of occupation. For drivers the S.M.R. is lowest for bus drivers (82), perhaps because of medical selection in the issue of public service vehicle licences, and highest for tram and trolleybus drivers (114), perhaps because the replacement of trams by buses in the years 1949-53 involved some adverse medical selection of those continuing as tram drivers. Intermediate S.M.R.s were recorded for drivers of goods vehicles (91) and other passenger vehicles (98).

Bus and tram conductors showed an S.M.R. of 97. Conductors showed a lower S.M.R. than bus drivers for coronary diseases but higher S.M.R.s for tuberculosis and bronchitis. Deaths from cancer of the lung were higher than expected among drivers of "other" passenger vehicles and goods vehicles but not among drivers of buses or of trams and trolleybuses nor among lorry drivers' mates and not significantly among conductors.

The figures for water transport workers are affected by deficiencies in the census returns for the merchant navy and probably by some overstatement on deaths of the status of dock labourers. The deaths of dock labourers were nevertheless above expected under the headings of tuberculosis, cancer, bronchitis, pneumonia, stomach ulcers, and accidents not in the home. Deaths from coronary diseases were below expected.

As for the merchant navy, the census returns for aircrew were deficient. Excluding aircrew and managerial workers, only 40 deaths were recorded among air transport workers.

Among workers in communications, managerial and supervisory workers and radio, telegraph, and telephone operators experienced an excessive number of deaths from coronary disease but of these only telephone operators returned a significantly high S.M.R. for all deaths. Postmen and Post Office sorters returned an S.M.R. of 93 but their mortality was significantly above the average for cancer of the lung and bronchitis.

C. J. CORNWALL

BOOK REVIEWS

Ministry of Labour Gazette, Vol. LXVI, No. 8, August 1958. **The Work of the Industrial Rehabilitation Units.** (1*s.* 9*d.*). London: H. M. Stationery Office.

Here and there, sparsely distributed in the industrial areas of Great Britain, you will find an industrial rehabilitation unit. Anything with a name like this is certain to be paid for by a government department. In this instance it is the Ministry of Labour.

There are 15 of these units designed to reinforce, by a period of training, the prospects of employment for the physically and mentally handicapped. To gain admission you need not necessarily live within daily travelling distance, for 284 of the 1,600 places available carry a residential scholarship, as it were. Moreover in a number of places lodgings are available for trainees, but seen as a statistic you are less likely to stay the course if you are a lodger.

Various aspects of the work of these units have been reviewed before. In this report the Ministry answers such questions as, Where do they come from? What is wrong with them? How do they last out the course and how do they make out afterwards? They are analysing 9,608 people (8,262 males and 1,346 females) who knocked and were admitted during 1956.

From the rather sticky mess of figures and tables from which you can gain the complete answers if you can afford the time to fiddle, certain salient facts emerge.

(1) Seventy per cent of the entrants come from medical sources, half of them from hospitals. (2) The rest come from employment exchanges and half of these are permanently disabled. (While the Report suggests that the referral from doctors could well be stepped up it insists that some of the intake should still be reserved for the employment exchange.) (3) Those who have suffered from tuberculosis form by far the largest group. (4) The psychoneurotics are the next largest and after them come the heart cases. Injuries of upper and lower limbs together about equal the heart cases. Entries suffering from psychiatric disabilities have shown an upward tendency in the last five years and together accounted in 1956 for 17% of all entries. The increase is most marked in the psychotic group, possibly because lately the industrial rehabilitation units have admitted patients direct from mental hospitals before their discharge, an arrangement that the Piercy Report recommended be extended.

(5) Nineteen per cent of all entrants fail to complete the course, over half for medical reasons. The least likely people to give up are the tuberculous and the most likely, the psychoneurotics. (6) Of those completing it, 82% were placed in work or started training within six months. Those suffering from injuries of the upper and lower limbs and the tuberculous were easy to place; the arthritics, the heart cases, and the mentally deficient were relatively difficult.

(7) Six months after leaving, the welfare authorities write and ask, "How are you getting on?" Of those who replied among those under review, 62.4% said in effect "I'm in work and I like it." If you now ask,"Ah, but how many replied", I believe the answer is there somewhere but it is not obvious.

My impression is that these units are certainly achieving their objective. At least some of the handicapped are being offered a lift and we should all rejoice. The factors influencing success are obviously complex. The tubercle cases do the best, but are probably more carefully selected by the chest physicians than most entrants. They are also younger. Those who have been out of work a long time before starting the course are harder to rehabilitate than those who have only been out for a short time. That is not surprising. When it comes to finding a job again the illiterate and those with little schooling are harder to place. Nor is that surprising in a scientific age.

It is interesting and perhaps surprising that 500 patients who had a claim for compensation pending did rather better than the others. Possibly the person under the shadow of a fortune from misfortune never consents even to knock at the door of an industrial rehabilitation unit.

There is one further item worth recording. Youth employment officers are allowed to send a number of badly handicapped young people to an industrial rehabilitation unit for a short vocational assessment by the industrial psychologist which may take from one to five days. Two hundred and twenty-eight young persons were assessed in the 14 months, October, 1956, to October, 1957, and three months after assessment 65% of them had been placed in open employment. Good.

TOM GARLAND

Cardiovascular Rehabilitation. Edited By Paul Dudley White, Howard A. Rusk, Bryan Williams, and Philip R. Lee. (Pp.vii + 155. 50*s.* 6*d.*) London, New York, Toronto: McGraw Hill. 1957.

This is a lightly edited report of a two-day conference held in New York in May, 1956. The first two editors were co-chairmen at the conference and the last two were conference coordinators. There were 31 other participants representing cardiology, physiology, public health, industrial health, physical medicine, rehabilitation, and psychiatry.

The objectives were to state "the major problems facing the practising physician", the "major areas of current and future research", and the educational requirements of public, physicians, and other personnel

in relation to the rehabilitation of patients with cardiovascular disease. For this purpose presentation and discussion were conducted under the five headings of "Emotions", "Work", "Practice of Cardiovascular Rehabilitation", and "Teaching and Research", and these form the separate chapters of the book.

Time and space were too short for a fully supported dissertation from any one contributor on any of the very numerous aspects brought up and ventilated. However there are over 500 references.

No one will be surprised that diametrically opposed opinions were expressed about almost everything and that although many questions were raised few could be dogmatically answered. A notable exception was the general agreement that the definition of rehabilitation should include restoration of both mental and physical activity. With this no one could take exception, and indeed most people would agree that the mental aspect of rehabilitation is as important as the physical aspect.

The conference underlined the absence of a simple clinical test for gauging the physical stress that an individual may experience without harm and pointed out that the patient's own opinion on the effects of work that he has just done or attempted to do may be quite inaccurate in terms of too little or too much, depending to some considerable extent on his mental attitude.

Everyone will agree with Dr. Benton when he states "that a man with a catheter threaded into his heart, a Cournand needle in his femoral artery, a continuous infusion running into his arm vein, a catheter in his urethra, feet on the pedals of a bicycle, and lying on his back on a fluoroscope table in a darkened room, must be considered as being in somewhat other than a basal state!" But it is surely to be hoped that some of these methods of investigating reaction to work load, together with more accurate methods of estimating work load itself, may lead, as so often in the past, to the dispensing with these complicated procedures and the establishment of simpler accurate tests.

With so little known and agreed on the basic factors it is reassuring to hear from Dr. Franco that 70% of all acute "coronary" cases occurring in his factory return to work, often without change of job (only 5-7% are retired) and more recently from Dr. Hellerstein* that 75% of all subjects attending his (and other) cardiological work classification units return to competitive work to the satisfaction of themselves and their employers.

The importance of cardiologist, general practitioner, industrial medical officer—as well as the general public—becoming rehabilitation minded is stressed. In this connexion the undergraduate is the main target. The role of medical school, work classification unit, public health authority, and industry in education and research is discussed and progress reports of some of the recently initiated programmes are briefly given.

This book has the advantages of brevity. The disadvantages are met by the very adequate bibliography. It is an excellent introduction to the problems of cardiovascular rehabilitation in the U.S.A. today and to some of the ways in which these problems are being tackled.

AUBREY KAGAN

*H. K. Hellerstein (1958) *Circulation*, p. 114.

Report of the Survey of Paraplegic Mineworkers. Under the direction of Alan G. Hardy. (Pp. 82). London: Coal Industry Social Welfare Organization. 1957.

This report reviews 497 mine workers, 97% of whom had been underground workers who suffered from traumatic paraplegia. In the main the report examines the social problems attendant upon and the welfare services available for this condition.

It is surprising to learn the degree of independence achieved by these men. Despite half the cases having complete paraplegia (the other half had varying degrees of partial paraplegia) only 27 men were confined to the house. No fewer than 409, or 83%, were able to go out alone.

There are many other tables in the report concerned with nursing care, bladder and bowel control, etc., but probably one of the most useful functions of the report is to spotlight the inconsistencies shown by various ministries and local authorities, both with regard to procedure and speed of action. The inconsistencies are particularly applicable to speedy provision of motorized wheel chairs, widening of doors, provision of hand rails, and charges by local authorities for the provision of mattresses and bedding. A standard procedure should be laid down which allows prompt attention to these matters instead of the frustrating delays which now obtain.

The degree of cooperation between the National Coal Board and the National Union of Mineworkers is highly commendable in the way that washing machines, television sets, and holidays are provided.

Finally, there is a plea for the provision of facilities for paraplegics who are willing and able to earn a living.

This report may have a limited appeal to industrial medical officers but some of the problems which are spotlighted are applicable to other forms of disability and other industries.

R. A. TREVETHICK

L'Acide Sulphurique et ses Dangers (Sulphuric Acid and its Dangers). By A. Vallaud and P. Salmon; Foreword by Dr. Henri Desoille. (Pp. 180; 71 figures, 1 colour plate. Fr. fr. 300.-.) Paris: Institut National de Sécurité pour la Prévention des Accidents du Travail et des Maladies Professionelles. 1957.

This useful monograph forms one of a series on the practice of industrial hygiene, prepared by l'Institut National de Sécurité in France. Previous monographs dealt with benzol, carbon monoxide, dermatoses in the metal industry, and chlorinated solvents. The authors of the present volume, A. Vallaud and P. Salmon, are respectively chief of the technical services and engineer to the Institute. In six chapters they give a remarkably complete account of the dangers attending the manufacture, handling, and use of sulphuric acid in industry, beginning with a recapitulation of the physico-chemical properties of the acid, and the conditions under which accidents arise. Though they are not medically qualified, they also deal with the toxicology and treatment of acute and chronic poisoning by sulphuric acid. This section is adequate but not authoritative, and the authors are

on much firmer ground when they discuss the safety measures which should be put into operation in places where the acid is handled and transported, and also the methods of preventing fire and explosion. There is a particularly full account of the various materials which are acid-resistant and so can be used for acid containers, pipes, and joints. These materials range from the metals and alloys to glass, enamels, rubber, ebonite, and the various plastics, including polyvinyl chloride and polytetrafluorethylene (P.T.F.E. or teflon). The authors state that it resists sulphuric acid of all strengths and oleum (20%) up to high temperatures. Its only disadvantage, they say, is its high cost. Perhaps it would have been better to define what is meant by high temperatures, because in the region of 200°C. P.T.F.E. begins to decompose and give off toxic gases.

The methods of storing, handling, and transport of sulphuric acid are given in great detail, and in the section on tank wagons reference is made to the manual on acid handling issued in 1950 by the Imperial Smelting Co. of Avonmouth. The dangers of emptying acid from such wagons by compressed air is emphasized and the special I.S.C. tank-wagon designed for emptying by gravity and pumping is commended.

A final chapter describes the principles of construction and maintenance of factories in which sulphuric acid is made and handled. An appendix gives details of the laws and regulations in force in France relating to the corrosive acids. The book is well produced and arranged, and for those who understand technical French terms it is clearly written. It is illustrated with 71 photographs and line drawings, some of them in colour. Of unusual interest are the photographs of an insect *Sirex Gigas* L. and a lead acid container through which it has burrowed. The insect is found in regions were conifers grow, and lays its eggs in these resinous woods. The insect, after maturation, forces its way out by tunnelling through the wood, and if a lead pipe or container is in the way it will go through the lead as well. Leakages of acid have been reported as a result of the insects' activity, and it is recommended that all resinous wood used in chemical factories to support lead containers and pipes should be treated with insecticides.

The authors say in their concluding paragraph that the book is designed to be read by management, foremen, and workers; but it would be equally useful for other groups of people who are concerned with industrial hygiene. It is obvious that if it is to be widely read in this country, it should be translated into English.

A. I. G. McLAUGHLIN

Recent Outbreaks of Infectious Diseases. By S. Leff. (Pp. ix + 408; 2 figures. 35*s*.) London: H. K. Lewis. 1957.

Among the most exciting parts of the history of medicine are the stories of epidemics. Cholera in Broad Street or Hamburg, the odd escapes of the brewers who probably drank no water, or of the classy inhabitants of Altona are as good an introduction to epidemiology as is the Devonshire colic story. Devotees of Snow or George Baker are often reluctant to admit that the epidemics of today are exciting too. Dr. Leff's book should convince them that they are. It is divided into three parts: recent outbreaks of virus disease, of bacterial disease, and some good examples of disease due to relatively inert substances, lead poisoning, and atmospheric pollution. The inclusion of this latter section (a new and welcome departure in a book of this type) is not reflected in the title which is in consequence misleading.

Among the infections pride of place is given to the big threat of smallpox and most of the really interesting facts about recent explosions are described. Localized outbreaks of polio, Q fever, psittacosis, and Bornholm disease follow. The enterics and food poisoning are given a large section and diphtheria a relatively short description, though the fascinating series of cases in South Staffs in the early 1950s are described in detail.

Outbreaks of non-infectious disease are often just as much of a challenge to the epidemiologist as are the infections. Exciting examples, such as retrolental fibroplasia, are not hard to find and it is a pity that the author has limited himself to lead and to fog. Almost all of these community case histories have been published before and Dr. Leff is clear in his references, but it is the bringing together of stories so dissimilar yet with so many common features that is the particular usefulness of this book.

There are two conflicting features which the author has tried to reconcile: one is the "text book" aspect of the book, the formal description of the disease, its diagnosis and treatment. The other, and much more interesting aspect, is the description of the outbreaks themselves. It is possible that some details (and even some descriptions) may have been sacrificed for the sake of providing a bit of text book revision. This is a pity for the main work is exciting and useful.

E. M. BACKETT

Industrial Health: A Survey in Halifax. A report by H.M. Factory Inspectorate and recommendations of the Industrial Health Advisory Committee. (Pp. 20. 1*s*. 6*d*.) London: H.M. Stationery Office. 1957.

In this country advances in occupational health and welfare have usually followed the raising of standards set by the more enlightened employers. After a time lag of variable duration the legislature has accepted these standards as minimum requirements but in the interval further progress by the enlightened has been made. It is therefore not unexpected that there should be a wide disparity between environmental conditions and medical services in the good and not so good factories and it is not surprising that the progress of industrial health should be a series of steps rather than a continuous steady trend.

The report by H.M. Inspectorate of a survey of industrial health in Halifax illustrates how poor conditions in many factories and workshops can be and there is reason to believe that conditions in Halifax are not untypical of those existing throughout the contry. This report is at one and the same time a criticism of the Inspectorate that the conditons revealed could be so bad, and a tribute to its integrity that no attempt has been made to suppress or gloss over information which the

survey has revealed. Quite obviously this department of the Ministry of Labour is grossly understaffed for it has, for a long time, been common knowledge amongst industrial medical officers and appointed factory doctors that conditions, especially in many small factories, are deplorable, and that many of the provisions of the Factories Acts are not being met. The Halifax Report therefore is valuable in that it officially discloses the facts on which to base decisions for future action. One omission, however, concerns the statutory examination of young persons. Apparently no attempt was made to determine whether the law in this respect is being universally respected. Many appointed factory doctors can testify that to their knowledge some occupiers, especially of small factories and workshops, overlook or ignore their responsibilities to have their young people examined within a fortnight of entry to their employment and thereafter at yearly intervals until the age of 18. It was perhaps outside the scope of the enquiry to comment on the value of these examinations as at present conducted, but such a discussion must surely soon be initiated.

One issue which seems to arise rather acutely from the Report is that of the nature of medical supervision in industry. Tribute is paid to much of the excellent work which is done in Halifax but the comment is made that the "supervision tended to be a clinical one . . . while observations on environmental conditions and of individuals actually at work, ..." were much less in evidence. Elsewhere the suggestion has been made that the Public Health Service might undertake much of this work, but the failure of that service generally to carry out its statutory duties with regard to the inspection of sanitary arrangements in factories suggests that medical officers of health and their colleagues are insufficiently interested in the problems of industrial health to be entrusted with further responsibilities in this field. This then poses the problem of the organization of an industrial medical service, its function and nature, and the training of the doctors and auxiliaries engaged in it. It is greatly to be hoped that these questions will be answered on the merits of the case put forward and not on preconceived doctrinaire notions. The facts as presented in the Halifax Report together with those we may expect from a survey of the potteries will make a notable contribution to this discussion.

JAMES A. SMILEY

The Practice of Industrial Medicine, 2nd ed. By T. A. Lloyd Davies, with a chapter on the *Hazards of Coal Mining* by John Rogan. (Pp. vii + 282; 15 figures. 30*s*.) London: J & A. Churchill. 1957.

The second edition of this book fulfils the need even better than the first for a concise guide to those entering industrial medicine or nursing. The aims, philosophy, and day-to-day practice of industrial medicine are ably and wisely presented. Nearly half the book is devoted to the common clinical and environmental problems of the doctor and nurse in industry as opposed to the specific occupational diseases which, in practice, are much less time consuming. There is no attempt to treat individual subjects exhaustively, but comprehensive bibliographies follow each section which mention most of the authoritative literature. Two notable omissions in the bibliographies are "The Functions of an Occupational Health Service in an Industrial Organization" published by the Association of Industrial Medical Officers, in the section dealing with the duties of an industrial medical officer, and the valuable hygiene guides published by the American Industrial Hygiene Association in the section on diseases due to chemical causes.

The weakest section is that on absenteeism and illness. There is no mention of the modern developments in the recording of industrial sickness absence statistics, of the International Statistical Classification of Diseases, Injuries, and Causes of Death (W.H.O., 1958), which for all practical purposes has replaced other classifications, or of the opportunities for epidemiological research in industry. It is misleading to suggest that older workers have less sickness absence than younger workers when most published work supports the opposite view.

There is, however, one general criticism of an otherwise valuable book. By the stress on the grossly unsatisfactory working conditions and the resistance by industrialists to improvements in the "bad old days", the impression is given that the industrial medical officer's main problem is still to persuade employers of the necessity and value of improvement. In practice, a common difficulty is to persuade the employees, and especially their representatives, of the desirability of change. The author continually and rightly emphasizes the impartiality of the doctor in industry, but this impartiality must also recognize that faults which doctors can help to correct are not now all on one side.

P. A. B. RAFFLE

Tenth Annual Report 1956-57 and a Review of the First Ten Years. (Pp. 76; illustrated.) The Slough Industrial Health Service Ltd. 1958.

This report is a remarkably full one and describes in greater detail than usual the varied work carried out during the year. The firm is a non-profit making limited company with charitable objects; the governing council includes representatives of the Slough Trades Council, the Ministries of Health and of Labour, the Nuffield Foundation, the University of London, and industrial managements.

The aim throughout has been to meet the industrial health needs of those working locally in both small and large firms. Special objectives were to investigate and control environmental hazards, to provide good rehabilitation, and to blend with the other health services generally available. Although there have been some minor disappointments, which are acknowledged in the report, it is clear that a high measure of success has been reached. Good liaison with the local hospitals, particularly in respect of injuries, has led to sharing with them many facilities, including *x*-ray examinations, physiotherapy, and chiropody, while certain hospital specialists have been appointed to the Service in a part-time capacity. The general practitioners in the district, after some early difficulties had been overcome, now largely welcome the help that the Service can provide for their patients.

A particularly interesting section of the report deals

with the development of the occupational hygiene service. In 1956 it became necessary to relinquish the laboratories at the London School of Hygiene and new accommodation for the team responsible for this work has now been provided in a building adjacent to the central clinic at Slough.

The Chairman of the Council of Management, Sir Noel Mobbs, has contributed a brief review in a forward, and speaks of last year being outstanding in that it marked the completion of the new clinic at a cost of £60,000 subscribed by manufacturer members and by other interested bodies. His remarks are particularly interesting as he writes not only of what has been done to ensure safe and healthy working conditions, and the treatment of the injured and sick, but also of the financial cost. It is clear that at Slough close attention has been given to this matter of expense, on which all need to be well informed when advocating extensions of health supervision to those at work.

M. F. HUDSON

Digest of Statistics Analysing Certificates of Incapacity 1954/55. (76 tables, 2 charts). London: Ministry of Pensions and National Insurance. 1957.

The fourth annual digest of statistics of the Ministry of Pensions and National Insurance covers the period June, 1954, to June, 1955. As in previous years, the spells of sickness, injury, or prescribed disease for which benefit is payable are analysed by different combinations of age, sex, occupation of the claimant, regional and seasonal variation, duration of spell, and certificated diagnosis. Many will again be grateful to the Ministry of Pensions and National Insurance for their painstaking compilation. The considerable interval of nearly three years between the period to which the digest relates and its completion is no doubt some measure of the labour involved.

According to the introduction the Digest is intended primarily for "medical and social research workers and administrators". The first two classes of user will be disappointed at the incomplete information on the population at risk which occupies only four out of the 76 tables. More tables showing a breakdown of the data by age would also be welcome, and are indeed essential for the critical use of data of this kind. There is, for example, no table with an analysis by both age and locality. Spells of absence due to accidents are analysed by age and by industry (Tables 41-42); populations are given (Table 74) but there is no analysis of these by age. The number of claimants (a rather odd index) is analysed for selected occupations and most frequent cause (Tables 31-2) and again for selected causes and most common occupation (Tables 33-4) but no corresponding populations or age analysis are provided.

On the other hand the multiplicity of tables arising from the separate tabulation of days, spells of sickness, and number of claimants is at any rate from the epidemiological standpoint superfluous. One type of index, such as number of spells of sickness, analysed in greater detail, with exactly corresponding populations at risk, would be far more useful.

The "Index of Tables" in Appendix VII is confusing and could with advantage be replaced by an initial list of tables such as precedes the Registrar General's publications. In reviewing the Digest it was found desirable to make such a table for ease of reference.

No doubt the Ministry have to reconcile the conflicting claims of different users, and it is easy to suggest how some could be better served at others' expense. But the advances in medical knowledge gained in recent years through the epidemiological and statistical approach, and the growing recognition of the value as well as of the scarcity of sickness absence data justify a plea to the Ministry to re-deploy their resources for the benefit of research workers in planning future editions of the Digest.

A. S. FAIRBAIRN

Incentive Payment Systems. By R. Marriott. (21*s*.) London: Staples Press. 1957.

In his book of just over 200 pages Mr. Marriott has set out to bring scientific thought and investigation to bear on a subject which has numerous ramifications, many of which complicate research.

He discusses the aetiology of incentive payment systems, classifies them, and discusses their pros and cons and at the end of the book gives a general appraisal followed by an appendix listing the "basic requirements" of "sound" incentive payment systems. This will prove useful to those engaged in their practical application.

He draws freely on the opinion of people in management, trade union, and research appointments, and for this reason much of the book consists of quotations hung together with the author's remarks in between; this tends to interrupt the flow of thought when reading the book but may well be the only means of bringing some sort of homogeneity to a subject on which there have been many different views expressed, often with very little concrete evidence in their support.

This book will give the uninitiated a good all-round view of incentive payment systems, will help to bring into true perspective the ideas of those who may have dogmatic opinions, and may sound a warning to the young industrial executive who believes that human beings will react like machines provided the materials and organization are there.

To doctors it will serve to emphasize once again that man is an unpredictable animal not destined to react in any particular way to any particular set of circumstances.

This is a clear, concise work to which much thought and research has been applied.

At the end of the book one feels that opinion on the value of incentive payment systems has hardly begun to crystallize.

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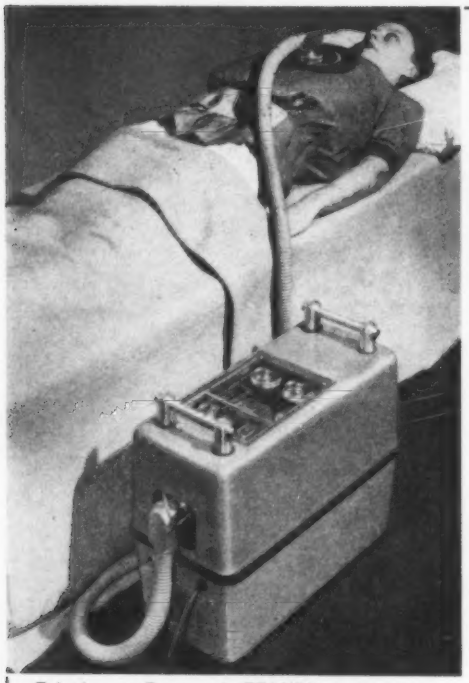

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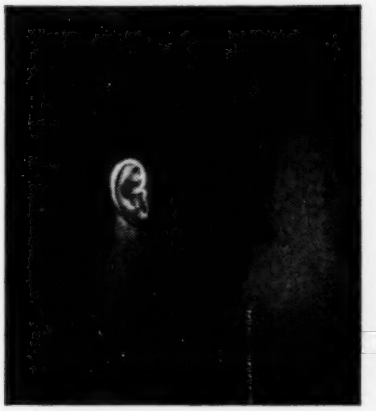

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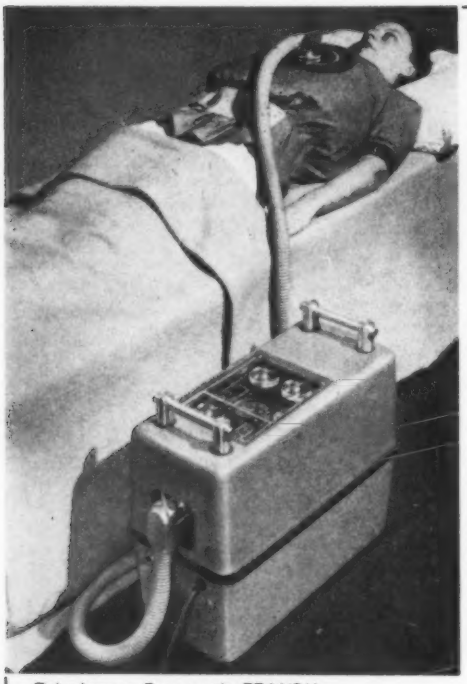

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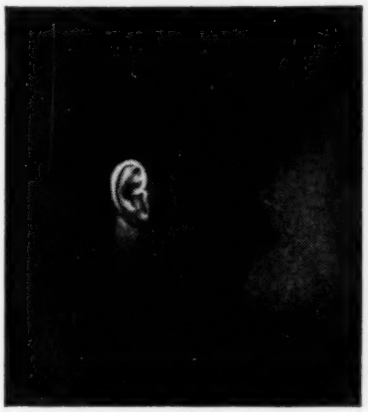

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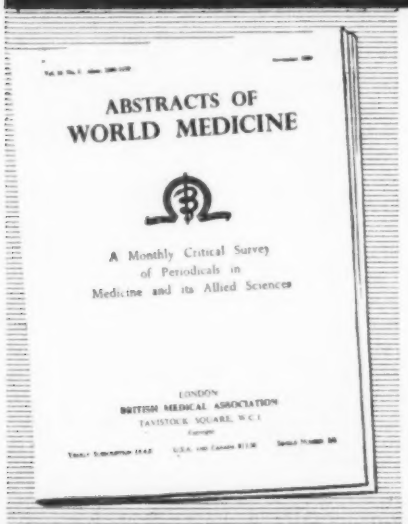

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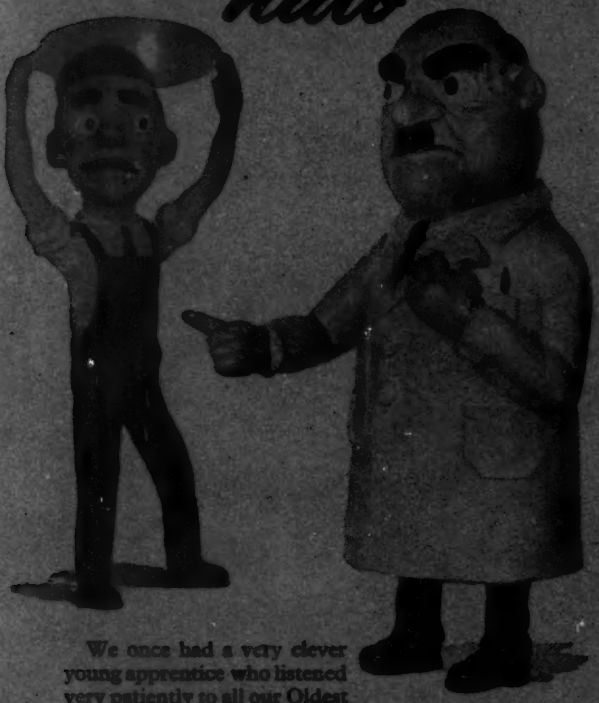

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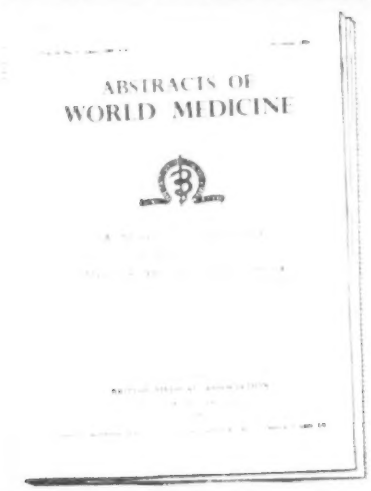

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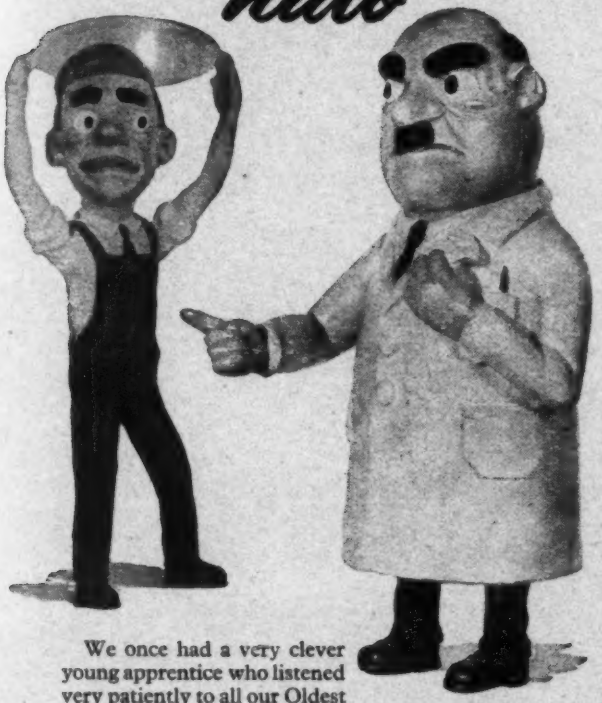

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